Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Acceptability for Continuing Registration

PACR2005-01

Re-evaluation of the Lawn and Turf Uses of (2,4-Dichlorophenoxy)acetic Acid [2,4-D]

The purpose of this document is to inform registrants, pesticide regulatory officials and the Canadian public that the Pest Management Regulatory Agency (PMRA) has re-evaluated the lawn and turf uses of the herbicide (2,4-dichlorophenoxy)acetic acid, commonly known as 2,4-D, pursuant to Section 19 of the Pest Control Products Regulations. This Proposed Acceptability for Continuing Registration (PACR) document provides a summary of the data and information reviewed, and the rationale for the proposed regulatory decision.

The PMRA has concluded that the use of 2,4-D to treat lawns and turf does not entail an unacceptable risk of harm to human health or the environment. Standard precautionary statements and label improvements are recommended.

By way of this document, the PMRA is soliciting comments from interested parties on the proposed regulatory decision for lawn and turf uses of 2,4-D. The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed decision. Please forward all comments to the Publications Coordinator at the address below.

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Foreword

The PMRA has completed a re-evaluation of the lawn and turf uses of the herbicide (2,4-dichlorophenoxy)acetic acid, commonly known as 2,4-D. This re-evaluation, initiated pursuant to Section 19 of the Pest Control Products Regulations, is part of the PMRA's commitment to review the most common lawn and turf chemicals used in Canada under the *Action Plan for Urban Use Pesticides*[1].

The PMRA has carried out an assessment of available information and has found it sufficient, pursuant to Section 20 of the Pest Control Products Regulations, to allow a determination of the safety, merit and value of the use of 2,4-D for application to lawns and turf. The PMRA has concluded that the use of 2,4-D and its end-use products to treat lawns and turf does not entail an unacceptable risk of harm to human health or the environment. Standard precautionary statements and label improvements are required. The addition of buffer zones to commercial products applied by tractor-pulled sprayers is also required to protect surrounding broadleaf vegetation.

The PMRA will accept written comments on this proposal up to 60 days from the date of this document to allow interested parties an opportunity to provide input into the proposed re-evaluation decision for these products.

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[1] More information on this action plan can be obtained at http://www.healthylawns.net

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1.0 Purpose

This document describes the outcome of the PMRA's re-evaluation of the herbicide (2,4-dichlorophenoxy)acetic acid, commonly known as 2,4-D, and its end-use products for use on lawns and turf in Canada. The assessment considered the potential impact of 2,4-D on the health and safety of users and others incidentally exposed when products are used on residential lawns, the potential environmental impact associated with use of 2,4-D, and its value as a herbicide in the maintenance of lawn and turf.

This re-evaluation was completed as part of the PMRA's commitment to review the most common lawn and turf chemicals used in Canada under the *Action Plan for Urban Use Pesticides*.

2.0 Background

2.1 Assessments in re-evaluation

The PMRA is currently re-evaluating all pesticides that were registered prior to 1995. As outlined in Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, the PMRA's re-evaluation program uses a modern scientific approach to determine whether older active ingredients continue to be acceptable in relation to their potential effects on human health and safety, and their potential impact on the environment.

Health and safety assessment
Re-evaluation involves a comprehensive review of the scientific data available on each pesticide. The health and safety assessment includes consideration of sensitive groups and their specific exposures (i.e., the sensitivity and exposure of children). It also applies additional safety factors to protect vulnerable groups and considers aggregate exposure to the same pesticide from all sources and routes of exposure.

Environmental assessment
The environmental assessment uses a tiered approach. The first tier identifies hazards to non-target organisms and those organisms in the environment that could be at a very high risk. The first tier usually overestimates risks. When a pesticide fails the first tier, which indicates that risks could be unacceptable, a more refined assessment (higher tier) will be conducted to more realistically define the magnitude and probability of risk.

Value
The PMRA seeks to understand, as early as possible in the re-evaluation process, the current uses of products under review and their importance for pest management. The PMRA relies to a great extent on provincial and territorial government input. Registrants and users are also an important source of information.

2.2 Information used in this assessment

Information considered by the PMRA in the assessment of 2,4-D included proprietary data from individual registrants, as well as the Industry Task Force II on 2,4-D Research Data, the Pesticide Handlers Exposure Database, the Outdoor Residential Exposure Task Force (ORETF), the Broadleaf Turf Herbicide Transferable Foliar Residue Task Force and published studies. A list of published studies for 2,4-D is included in the References section of this document.

2.3 Regulatory history of 2,4-D

2,4-D was first registered in Canada in 1946 and has been labelled for use on lawn/ turf since the 1960s. On lawn and turf, it is usually used in combination with one or more synthetic auxin herbicides that improve efficacy on certain weeds and broaden the weed control spectrum. The predominant combination is 2,4-D/mecoprop/dicamba. The first coformulation product containing 2,4-D/mecoprop/dicamba was registered in 1947.

The first Canadian re-evaluation of 2,4-D was announced in 1980 under the authority of Section 19 of the Pest Control Products Regulations. A re-evaluation of 2,4-D was undertaken in view of this product's broad range of applications and long history of use. It resulted in the identification of substantial data deficiencies that have since been filled by the key manufacturers of 2,4-D. A large number of more modern studies have been conducted, which have generated chemistry, mammalian toxicology, residue/metabolism, exposure, environmental toxicology and environmental fate data, to support the continued registration of 2,4-D in Canada and other countries, including the United States.

In 1994, Canada announced a label improvement program for 2,4-D products in Note to CAPCO C94-08, *2,4-D Re-evaluation Update and Label Improvement Program*, in order to increase the protection of the public and those who apply 2,4-D. More stringent requirements were added to protect users and agricultural workers (requirements for protective clothing and equipment, operator use precautions, mechanical transfer systems, preharvest intervals), the environment (information on drift, buffer zones, and upgraded aerial application instructions) and to increase public protection (re-entry intervals for turf, reduced maximum application frequency and maximum allowable application rates).

In September 2000, the PMRA published the *Action Plan on Urban Use Pesticides*, which gave priority to re-evaluating the lawn and turf uses of a number of pesticides. That month, the PMRA also formally announced the re-evaluation of the most commonly used lawn and turf pesticides, including 2,4-D, in Re-evaluation Note REV2000-04, *Re-evaluation of Lawn and Turf Uses of Pesticides*. In this document, the PMRA indicated that the review of the lawn and turf uses for 2,4-D would proceed in advance of the completion of the overall re-evaluation for 2,4-D, which will include all of its agricultural uses. The re-evaluation of the agricultural uses of 2,4-D is ongoing and will be the subject of a separate document in the future.

2.4 External consultation for 2,4-D review

The PMRA convened an independent five-member expert Science Advisory Panel in June 2003 to comment on and provide input into the mammalian toxicology and exposure re-evaluations, the preliminary human health risk assessment as well as the environmental risk assessment of 2,4-D for lawn and turf use. The Panel was provided with the draft PMRA assessment and given an opportunity to seek clarification of issues. Panel comments were provided in a final report submitted to the PMRA in January 2004. The Panel comments were carefully considered by the PMRA and reflected, as appropriate, in this document. Appendix II provides additional details regarding the consultation process, and a summation of the key comments from the Panel report.

2.5 Definitions of turf and the scope of this review

The re-evaluation of the lawn and turf uses of 2,4-D has focussed on the assessment of risks resulting from the treatment of the following types of turf:

- sports and recreational turf such as turf in parks, playgrounds, golf courses[2], zoos, botanical garden and athletic playing fields;
- lawn turf such as turf planted in or around residences, public and commercial buildings including schools and cemeteries; and
- sod that is grown in sod farms and harvested for transplanting[2].

These types of turf are collectively known as fine turf, which may be maintained by homeowners or by professional applicators. Utility turf, also known as rough turf, is not included in this assessment. Utility turf is primarily intended for soil stabilization, requires less maintenance than fine turf and is usually maintained with commercial class products and equipment intended for large-scale application. Utility turf (i.e., roadsides; rights-of-way for railways, hydro installations, pipelines and highways; highway interchanges; airports; wasteland; and industrial parks) will be considered when agricultural uses of 2,4-D are re-evaluated.

2.6 Forms of 2,4-D

2,4-D is sold in a number of different amine salt or ester forms, all based on 2,4-D acid. Different forms facilitate absorption of the 2,4-D acid into the plant differently. The ester form increases the lipid solubility of the herbicide, which allows it to more easily penetrate the waxy cuticle of the plant leaf. The amine form greatly increases the water solubility of the herbicide, which is desirable when effective use of the product depends on uptake by the plant via the roots.

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2 Although excluded from the announcement of re-evaluation of turf uses (REV2000-04), the use of 2,4-D on golf courses and sod farms is addressed in the current assessment.

The parent acid is the herbicidally active portion of the form. The parent acid is what binds to the herbicide target site within the plant and causes plant death, while the amine or ester portion of the formulated product may allow for greater absorption into the plant. For example, when an ester herbicide penetrates the cuticle, enzymes remove the ester moiety to yield the parent acid. As a result, following absorption, the ester part of the form plays no direct role in herbicidal activity. Therefore, when assessing 2,4-D, the application rates were expressed in terms of the amount of acid equivalent per hectare (e.g., kg a.e./ha).

Other differences in the various forms of 2,4-D will be explained in the mammalian toxicology as well as the environmental toxicology and fate sections of this review. The names of the various forms of 2,4-D for lawn and turf use are listed in Table 2.6.1.

Table 2.6.1 Forms of 2,4-D included in this assessment

Grouping	Form
Parent compound	2,4-D acid
Salts[3]	DEA: diethanolamine salt DMA: dimethylamine salt
Low volatile esters	2-EHE: isooctyl ester (2-ethylhexyl ester, 2-octyl, 2-ethyl-4-methylpentyl) BEE: butoxyethyl ester (*or* butoxyethanol ester)

3.0 Re-evaluation of the turf uses of 2,4-D

3.1 Identity of the active substance and the end-use products containing it

Active substance: 2,4-D

Function: Herbicide

Chemical names:

IUPAC: (2,4-Dichlorophenoxy)acetic acid

CAS: (2,4-Dichlorophenoxy)acetic acid

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[3] The registrations of products containing the sodium salt form of 2,4-D have been discontinued by registrants and, therefore, are not addressed in this assessment. Existing product may be used until the expiry date, 1 June 2005.

CAS number: 94-75-7

Molecular formula: $C_8H_6Cl_2O_3$

Molecular weight: 221.0

Structural formula:

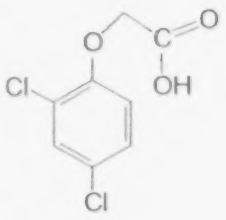

Table 3.1.1 Registration number, purity and registrant of the technical grade active ingredient (TGAI)

Registration number	Purity of TGAI[1]	Registrant
16981	97% (nominal)	Dow AgroSciences Canada Inc.
24836	74.8% (nominal)	Dow AgroSciences Canada Inc.
18611	96.0 (nominal)	Nufarm Ltd.
24562	96.0 (nominal)	Nufarm Ltd.
17134	94.0% (min.)	Nufarm Ltd.
17007	98.5% (nominal)	GroWell Ltd.
17044	98.5% (nominal)	Nufarm Agriculture Inc.
17045	99.0% (min.)	Nufarm Agriculture Inc.
17291	98.2% (nominal)	PBI/Gordon Corp.
27437	98.2% (nominal)	Albaugh Inc.

[1] Nominal guarantee (upper and lower limits), unless otherwise specified

The parent acid is the herbicidally active portion of the form. The parent acid is what *binds to the herbicide target site* within the plant and causes plant death, while the amine or ester portion of the formulated product may allow for greater absorption into the plant. For example, when an ester herbicide penetrates the cuticle, enzymes remove the ester moiety to yield the parent acid. As a result, following absorption, the ester part of the form plays no direct role in herbicidal activity. Therefore, when assessing 2,4-D, the application rates were expressed in terms of the amount of acid equivalent per hectare (e.g., kg a.e./ha).

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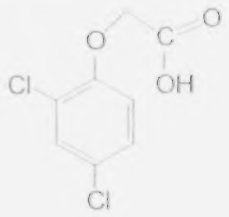

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17291	98.2% (nominal)	PBI/Gordon Corp.
27437	98.2% (nominal)	Albaugh Inc.

[1] Nominal guarantee (upper and lower limits), unless otherwise specified

3.2 Physicochemical properties of 2,4-D acid and interpretation

Property	Result	Interpretation
Vapour pressure at 25°C	1.87×10^{-2} mPa	Low potential to volatilize
Henry's Law constant	1.32×10^{-5} Pa m^3 mol^{-1}	Non volatile from water or moist surfaces
Ultraviolet (UV)/visible spectrum	Not expected to show significant UV absorption at wave length > 300 nm.	Low potential for phototransformation
Solubility in water at 25°C	**pH** **Solubility** (g/L) 5 20 7 23 9 34	Very soluble at all pH's
n-Octanol–water partition coefficient at 25°C	pH 5 Log K_{ow} = 0.04–0.33	Unlikely to bioaccumulate
Dissociation constant	pKa = 2.8	Dissociates rapidly to anion at environmental pHs

4.0 Effects having relevance to human health

4.1 Toxicology summary

The toxicology database for the various forms of 2,4-D in products for lawn and turf use consisted of proprietary and published studies conducted in laboratory animals. The various forms of 2,4-D registered for lawn and turf use in Canada include 2,4-D as acid, butoxyethyl ester (BEE), ethylhexyl ester (EHE), dimethylamine (DMA) and diethanolamine (DEA). All were assessed for acute and short-term toxicity in several mammalian species via various routes of exposure, as well as mutagenic potential, and developmental toxicity in rodent and non-rodent species. Mammalian metabolism and pharmacokinetic data were examined, and reproductive toxicity in rats as well as chronic toxicity and carcinogenicity in rats, mice and dogs were assessed using 2,4-D acid. Regulatory documents from the United States Environmental Protection Agency (USEPA), the Joint WHO/FAO Meeting on Pesticide Residues (JMPR) and the European Commission as well as peer-reviewed articles and other relevant publications were also considered, as were a number of expert assessments of the evidence available from numerous epidemiological studies on 2,4-D and other phenoxy herbicides.

3.2 Physicochemical properties of 2,4-D acid and interpretation

Property	Result		Interpretation
Vapour pressure at 25°C	1.87×10^{-2} mPa		Low potential to volatilize
Henry's Law constant	1.32×10^{-5} Pa m^3 mol^{-1}		Non volatile from water or moist surfaces
Ultraviolet (UV)/visible spectrum	Not expected to show significant UV absorption at wave length > 300 ηm.		Low potential for phototransformation
Solubility in water at 25°C	**pH** 5 7 9	**Solubility** (g/L) 20 23 34	Very soluble at all pH's
n-Octanol–water partition coefficient at 25°C	pH 5	Log K_{ow} = 0.04–0.33	Unlikely to bioaccumulate
Dissociation constant	pKa = 2.8		Dissociates rapidly to anion at environmental pHs

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A comparison of acute, short-term and developmental toxicity as well as the mutagenic potential indicated that the BEE, EHE and DMA forms of 2,4-D had similar toxicological profiles. However, certain quantitative differences were noted between 2,4-D BEE and 2,4-D acid, DMA and EHE, as evidenced by different no-effect levels in short-term toxicity studies. These differences in no-effect levels were taken into consideration as part of the risk assessment.

The DEA form of 2,4-D had a different toxicological profile compared to the other forms listed above. Available studies and foreign review summaries showed both a qualitative and quantitative difference in the toxicological effects that occurred after oral and dermal administration of the test article. Liver effects observed in a three-week dermal study in rabbits were not noted with the other forms of 2,4-D, and dietary studies indicated that 2,4-D DEA induced more severe thyroid and reproductive organ toxicity at lower dose levels when compared to all other forms of 2,4-D. Additional concerns arise from published data showing that repeated dermal application of DEA on its own is carcinogenic in mice (NTP 1997, 2001). No tumours were evident in a similar study conducted in rats, although the doses used were lower than those used in the mouse studies. In addition, short-term oral and dermal studies indicate that pure DEA causes brain and spinal cord demyelination in rats and is immunotoxic in rats and mice (NTP 1992a, 1992b, 1994). DEA is also classified as a List 2 formulant: potentially toxic formulants, with a high priority for testing (USEPA 2002b). Accordingly, the database for 2,4-D acid and the DMA, EHE and BEE forms of 2,4-D does not support the DEA form of 2,4-D. The registrant has submitted additional information regarding the toxicity of DEA on its own (as opposed to the DEA form of 2,4-D) to the PMRA for consideration. Mitigation measures for the DEA form of 2,4-D may be proposed depending on the outcome of the current review of this additional information.

4.1.1 Toxicology profile of 2,4-D acid, BEE, EHE and DMA

Available data indicated that all tested forms of 2,4-D were readily absorbed and excreted after oral administration. Peak plasma levels were attained four hours after dosing. Urine was the main route of excretion and tissue residues were low. The acid and amine forms were excreted unchanged, and 2,4-D esters (BEE and EHE) were rapidly hydrolysed to 2,4-D acid, which was excreted, unchanged, in the urine and, to a lesser extent, in the feces. Volatile metabolites of the esters were eliminated via expired air. Other metabolites of 2,4-D esters were recovered in the excreta. Despite the formation of other metabolites, 2,4-D esters and amine salts did not appear to impart higher toxic potentials or show different target organ toxicity relative to 2,4-D acid in acute and short-term toxicity studies.

Although the pharmacokinetics of 2,4-D showed some variability within and between species, allometric scaling of data from mice, rats, dogs and humans indicated that renal clearance of 2,4-D was approximately 30-fold slower in dogs compared to humans, making the dog less relevant as an indicator species for human toxicity. For this reason, the PMRA did not utilize the dog studies in the 2,4-D risk assessment.

Acute toxicity data from laboratory animals indicated that the various forms of 2,4-D were slightly to moderately toxic via the oral route of exposure. All forms of 2,4-D had low acute dermal and inhalation toxicity, but were severe eye irritants. 2,4-D DMA and EHE were irritating to skin, whereas other forms of 2,4-D were non-irritating. None of the forms were dermal sensitizers.

No systemic toxicity was noted in any of the short-term dermal studies in rabbits, using 2,4-D as acid, DMA, EHE or BEE. Short-term dietary exposure to 2,4-D at toxic doses adversely affected food consumption and body weight, and induced kidney and liver pathology. Higher doses in both short-term and long-term studies in the rat resulted in pathological changes in the liver, testes, ovary, uterus, adrenal, thyroid, thymus, bone marrow, lungs and eyes (retinal damage, cataracts). In all species, the primary target organ for toxicity was the kidney. Short- and long-term exposures via dietary administration induced similar effects and levels of toxicity in mice and rats, whereas dogs exhibited toxic effects at lower doses than rodents.

In vitro and in vivo test results showed that 2,4-D acid, DMA, EHE and BEE were not mutagenic or genotoxic; 2,4-D was not carcinogenic to either rats or mice. Results from these long-term toxicity and oncogenicity studies in mice and rats, which were conducted using 2,4-D acid in the diet, were considered applicable to the other forms of 2,4-D.

In 1991, a National Cancer Institute survey reported an association between dogs with canine malignant lymphoma (CML) and dog-owners who applied 2,4-D to their lawn (Hayes et al. 1991). However, a subsequent report by an independent panel concluded that the study design, analysis and interpretation were severely flawed and, in fact, did not show an association between CML and 2,4-D use (Carlo et al. 1992). Although a further set of analyses by the National Cancer Institute addressed some of the outstanding concerns (Hayes et al. 1995), a full re-examination of the 1991 data set by Michigan State University revealed an overestimation of the effect of 2,4-D due to misclassification of the exposure group ("unknowns" coded as positive). Furthermore, no differentiation was made between the number of times 2,4-D was used and the number of times other lawn care products were applied, the amount used or the type of application (i.e., spot versus full lawn treatment). Once this correction was made, the original association between 2,4-D use and CML could no longer be supported, and no relationship could be established (Kaneene and Miller 1999). Kelsey et al. (1998) report only a modest association between canine lymphoma and the use of lawn herbicides. A more recent study investigated the association between CML and living in industrial areas versus the use of chemicals (e.g., paints, solvents) by dog owners (Gavazza et al. 2001). This study concluded that pesticide use was either not associated with the disease, or was uninformative. The weight of this evidence, combined with the lack of any indicators for lymphoma in short- and long-term dietary studies in dogs, indicates that the original report of an association between homeowner use of 2,4-D and CML cannot be substantiated or supported.

In adult rats, neurotoxic effects were evident after a single high-dose exposure. The observed incoordination and slight gait abnormality were no longer evident four days later. Repeated high doses also affected forelimb grip strength and induced retinal degeneration. Published studies involving intraperitoneal and subcutaneous administration of 2,4-D acid to pregnant rats as well as studies focusing on oral exposure of pups through mother's milk during postnatal days 15–25, resulted in myelin deficiency in the central nervous system of pups. Another study using a combination of prenatal and postnatal exposures showed a delay in the development of the surface righting reflex, geotaxic response and hindlimb support in rat pups, which correlated with alterations in the development of the monoamine systems in the brains of these rats as adults (Bortolozzi et al. 1999, 2003; Duffard et al. 1995, 1996; Rosso et al. 1997, 2000; Sturtz et al. 2000). Although these effects were observed at much higher dose levels relative to the doses causing the primary target effects in the short- and long-term studies, these findings may be an indication of offspring sensitivity after exposure to 2,4-D during prenatal and postnatal development.

The potential for offspring sensitivity was also noted in the multigeneration reproductive toxicity study in rats, which showed significant effects on prenatal and postnatal pup survival at high-dose levels that were only marginally toxic to the dams. Although this rat study was deemed deficient for several reasons, the severity of the effects noted in the pups (i.e., mortality) relative to marginally toxic effects occurring in the dams may be an indication of selective sensitivity in the offspring. Other effects included a decreased sex ratio (more males) in the F_{1a} generation at the high dose, an increased gestation period, smaller litter size, and a marked increase in still births.

Developmental toxicity studies in rats and rabbits showed no indication of increased sensitivity in young animals relative to adult animals. Guideline studies indicated that 2,4-D acid, DMA, EHE and BEE did not cause birth defects in rats and rabbits. At maternally toxic doses, developmental effects observed in some studies consisted of delayed skeletal growth, skeletal variations and lower pup weights. With regard to published studies, fetal urogenital malformations have been observed in rats at maternally toxic doses, but these doses were generally above those used in the standard guideline studies (Fofana et al. 2002; Sulik et al. 2002). Although a preliminary study reported fewer fetal implantations in 2,4-D treated rats, errors in the study design negated the study authors' interpretation (Cavieres et al. 2002). In addition, a study using a coformulation of 2,4-D and picloram, which is not registered for turf in Canada, was negative for male-mediated birth defects (Oakes et al. 2002). An increased incidence of maternal death in pregnant rabbits indicated that rabbits were more sensitive than rats to the toxic effects of 2,4-D. The developmental toxicity studies, which used gavage dosing, often indicated a steep dose-response between serious effects (i.e., mortality, abortions) and the no-effect level. Although a similar response was not evident in the dietary studies, suggesting that the steep dose-response was attributed to bolus dosing, this observation remains of concern.

Both the potential sensitivity of young developing rats and maternal mortality in rabbits were considered in the human health risk assessment to ensure that adequate margins of safety were achieved. Reference doses for various population subgroups have been set based on no observed adverse effect levels (NOAELs) for the most relevant endpoints, namely effects on body weight, renal toxicity, neurotoxicity and maternal mortality. These reference doses incorporate various uncertainty factors to account for extrapolating between rats and humans, for variability within human populations and for data uncertainties. Additional safety factors have also been applied, where warranted, to protect pregnant females and their unborn children as well as nursing children from identified endpoints of concern.

4.1.2 Human evidence—cancer

Numerous epidemiology studies on 2,4-D and related chlorophenoxy herbicides have provided contradictory findings with respect to an association between 2,4-D and the development of soft-tissue sarcoma and non-Hodgkin's lymphoma. A number of experts and expert panels have examined these studies in detail and have concluded that while some of the studies suggest a possible association between 2,4-D exposure and an increase in these tumours in humans, other epidemiological studies fail to support such an association. In 1996, a USEPA Carcinogenicity Peer Review Committee examined the 2,4-D databases for both animal carcinogenicity and epidemiology. The Committee concluded that these studies did not provide sufficient evidence to merit changes to the conclusions previously reached and that 2,4-D should remain classified as a "Group D carcinogen" (not classifiable as to human carcinogenicity) (USEPA 1997a).

Since the release of the USEPA Cancer Peer Review Committee report in 1997 (USEPA 1997a), other assessments of the epidemiological and animal evidence regarding 2,4-D and cancer risk also indicated that there is inadequate evidence that 2,4-D is a human carcinogen (Gandhi et al. 2000; Garabrant and Philbert 2002). Other regulatory authorities that have finalized their assessments for 2,4-D include the World Health Organization (WHO/FAO 1996), the United States Department of Agriculture (USDA Forest Service 1999), the New Zealand Pesticides Board Expert Panel on 2,4-D (New Zealand, 2000), the European Commission (EC 2001), the Joint WHO/FAO Meeting on Pesticide Residues (WHO 2003) and the USEPA (USEPA 2005). All are in agreement that there is no evidence of carcinogenicity in the animal toxicity studies and that the epidemiology studies show no clear association between exposure to phenoxy herbicides and human cancers. The PMRA is not aware of any new evidence that would challenge these conclusions, and more recent epidemiological analyses lend further support for this classification (De Roos et al. 2003; Alavanja et al 2002, 2004). Because of the inconsistent epidemiological associations, the recognition that there are many other factors that may have contributed to the weakly positive associations and the fact that the animal studies designed to show causality were consistently negative, the PMRA concurs that 2,4-D cannot be classified as to its human carcinogenicity on the basis of all available and relevant data. However, the PMRA and the 2,4-D Science Advisory Panel concur

with the stated premise of Gandhi et al. (2000) that, as with any chemical, caution should be exerted in its use, storage and disposal.

4.1.3 Human evidence—reproductive effects

Several epidemiological studies have been published that examine possible reproductive and fetal effects in humans following exposure to chlorophenoxy herbicides. A study involving Ontario farmers reported detectable levels of 2,4-D in both semen and urine. However, a separate assessment to identify any association between chlorophenoxy herbicides and spontaneous abortions in Ontario farm populations indicated that Ontario farm families who participated were not at increased risk for spontaneous abortion. Risk estimates for early versus late spontaneous abortions indicated a moderate increase in risk for early abortions; however, the exposure could not be adequately characterized as the number of pregnancies was too small to also incorporate potential confounders of the exposure-disease relationship (Arbuckle et al. 1998, 1999a, 1999b, 2001; Savitz et al. 1997; Sever et al. 1997).

A series of studies conducted in four wheat-growing states in the United States have reported associations between general pesticide use and birth defects, with the most recent study reporting an association between high-wheat growing areas and certain birth defects. The high-wheat growing area was used as a surrogate indicator for chlorophenoxy herbicide exposure. However, this same study also reported that separate analyses showed similar increases in these anomalies in low-wheat growing areas as well, suggesting other factors need to be considered. In the absence of any direct measurements of exposure to 2,4-D, the current scientific evidence to support adverse reproductive and developmental effects in humans, in association with exposure to 2,4-D, remains unclear.

Interpretation of epidemiological results for potential cancer or developmental and reproductive effects were often confounded by factors such as the general grouping of 2,4-D with other pesticides (2,4,5-T[4], 2,4-DB, MCPA, MCPB, mecoprop, atrazine etc.), and, in older studies, pesticide contamination with TCDD[5]. This highlights the need for more precise epidemiological study designs with proper exposure characterizations to identify any specific associations between 2,4-D exposure and human health effects.

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4 Dioxin (TCDD) contamination of 2,4,5,-T was identified in the early 1970s and the manufacturing process was then improved to reduce this contaminant significantly (<0.5 ppm). 2,4,5-T, once registered in Canada for forestry use (not lawn and garden), has not been used in Canada since 1982. Registration was discontinued in 1985.

5 In 1983, the manufacturing process for 2,4-D was modified, and a production limit of "not detectable at 1 ppb" was established for 2,3,7,8-tetrachlordibenzo-p-dioxin (2,3,7,8-TCDD). Based on the current manufacturing process, the precursor phenol (2,4,5-trichlorophenol) that forms 2,3,7,8-substituted isomers is not used to manufacture 2,4-D. Furthermore, as a result of the review in 1981, improved methods of synthesis are employed to lower the levels of non-2,3,7,8-substituted dioxins in 2,4-D. Thus, with refined manufacturing processes, contamination of 2,4-D with dioxins and furans is not seen, nor is it expected.

4.1.4 Selection of toxicological endpoints for risk assessment

The toxicology endpoints used in the *risk assessment of 2,4-D are based on studies in* laboratory animals. These are summarized in Table 4.1.4.1. Reference doses for various populations and subgroups have been set based on NOAELs for the most relevant endpoints, namely effects on body weight, renal toxicity (the primary target organ), neurotoxicity and maternal mortality. These reference doses incorporate various safety factors (SF) or uncertainty factors (UF) to account for extrapolating between rats and humans, for variability within human populations and for data uncertainties. Additional safety factors have also been applied, where warranted, to protect children and pregnant females from the endpoints of concern indicated above. Reference doses for aggregate assessment were based on the NOAELs for common endpoints affected across the route-specific studies, which were not necessarily the study NOAELs.

Table 4.1.4.1 Toxicological endpoints used in the 2,4-D lawn/turf risk assessment

Endpoint	Population	2,4-D acid, DMA, EHE			2,4-D BEE		
		NOAEL (mg/kg/day)	Study	UF/SF or MOE	NOAEL (mg/kg/day)	Study	UF/SF or MOE
ARfD	Females 13–50	25	Rat developmental	300	Same as acid		
	GP children	75	Acute rat neurotoxicity	300	Same as acid		
ADI*	All populations	1	Two-year rat	300	Same as acid		
Short-term 1–7 day dermal and inhalation	Females 13–50	10	Rabbit developmental	1000	10	Rabbit developmental	1000
	GP children	12.5	Rat developmental	300	Same as acid		
Short-term 1–7 day incidental oral	Toddlers	12.5	Rat developmental	300	Same as acid		
Short-term 8–30 day dermal and inhalation	Females 13–50	10	Rat developmental	1000	10	Rabbit developmental	1000
	GP	12.5	Rat developmental	300	Same as acid		
Aggregate 1–7 day all routes	Females 13–50	10	Rat developmental	1000	10	Rabbit developmental	1000
	GP children	12.5	Rat developmental	300	Same as acid		

ARfD (acute reference dose); ADI (acceptable daily intake); Females 13–50 (females of childbearing age); GP (general population)

* The PMRA has recently received additional data from the 2,4-D Task Force that may further inform the ADI. These data will be fully assessed during the re-evaluation of 2,4-D for cumulative use. In the interim, the above ADI was established for the purpose of conducting an aggregate risk assessment.

Note: All endpoints were selected from studies with 2,4-D administered by the oral route. Dermal absorption is considered to be 10% of the oral dose and inhalation absorption is considered to be 100% (default value) of the oral dose.

4.1.4 Selection of toxicological endpoints for risk assessment

The toxicology endpoints used in the risk assessment of 2,4-D are based on studies in laboratory animals. These are summarized in Table 4.1.4.1. Reference doses for various populations and subgroups have been set based on NOAELs for the most relevant endpoints, namely effects on body weight, renal toxicity (the primary target organ), neurotoxicity and maternal mortality. These reference doses incorporate various safety factors (SF) or uncertainty factors (UF) to account for extrapolating between rats and humans, for variability within human populations and for data uncertainties. Additional safety factors have also been applied, where warranted, to protect children and pregnant females from the endpoints of concern indicated above. Reference doses for aggregate assessment were based on the NOAELs for common endpoints affected across the route-specific studies, which were not necessarily the study NOAELs.

Table 4.1.4.1 Toxicological endpoints used in the 2,4-D lawn/turf risk assessment

Endpoint	Population	2,4-D acid, DMA, EHE			2,4-D BEE		
		NOAEL (mg/kg/day)	Study	UF/SF or MOE	NOAEL (mg/kg/day)	Study	UF/SF or MOE
ARfD	Females 13–50	25	Rat developmental	300	Same as acid		
	GP/children	75	Acute rat neurotoxicity	300	Same as acid		
ADI*	All populations	1	Two-year rat	300	Same as acid		
Short-term: 1–7 day dermal and inhalation	Females 13–50	30	Rabbit developmental	1000	10	Rabbit developmental	1000
	GP/children	12.5	Rat developmental	300	Same as acid		
Short-term: 1–7 day incidental oral	Toddlers	12.5	Rat developmental	300	Same as acid		
Short-term: 8–30 day dermal and inhalation	Females 13–50	30	Rat developmental	1000	10	Rabbit developmental	1000
	GP	12.5	Rat developmental	300	Same as acid		
Aggregate: 1–7 day all routes	Females 13–50	30	Rat developmental	1000	10	Rabbit developmental	1000
	GP/children	12.5	Rat developmental	300	Same as acid		

ARfD (acute reference dose); ADI (acceptable daily intake); Females 13–50 (females of child-bearing age); GP (general population)

* The PMRA has recently received additional data from the 2,4-D Task Force that may further inform the ADI. These data will be fully assessed during the re-evaluation of 2,4-D for agricultural use. In the interim, the above ADI was established for the purpose of conducting an aggregate risk assessment.

Note: All endpoints were selected from studies with 2,4-D administered by the oral route. Dermal absorption is considered to be 10% of the oral dose and inhalation absorption is considered to be 100% (default value) of the oral dose.

4.2 Residential risk assessment

Residential risk assessment for lawn and turf use of 2,4-D encompasses the exposures that adults may receive while applying 2,4-D to their lawn as well as those adults and children may receive through contact with treated turf.

Residential risk is estimated by calculating a margin of exposure (MOE) based on comparing the potential exposure to the most relevant endpoints from toxicology studies. The calculated MOE is then compared to a target MOE, which incorporates safety factors protective of the most sensitive subpopulations. If the MOE is less than this target MOE, it does not necessarily mean that exposure will result in adverse effects, rather the absence of adverse effects is less certain. Mitigation measures are necessary to reduce exposure if MOEs are less than the target MOE.

4.2.1 Relevant toxicological endpoints and target margins of exposure for acute and short-term exposures to homeowners and children

For adults, the risk associated with a one-day (i.e., acute) exposure to 2,4-D was based on the most sensitive subpopulation, which, in this case, was females of child-bearing age (females 13–50 years) and the developing fetus. Protection of the most sensitive subpopulation is inherently protective of the general population. The most relevant endpoint for acute risk assessment was considered to be increased skeletal variations in rat fetuses noted in a rat developmental study. This is an endpoint that could potentially occur following a single exposure event. In this study, the NOAEL was 25 mg/kg bw/day acid equivalents (a.e.) based on increased skeletal variations noted at the lowest observed adverse effect level (LOAEL) of 75 mg/kg bw/day. The target MOE was 300 based on standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation) as well as an extra 3× safety factor to protect for potential sensitivity to the young noted in a series of published neurotoxicity studies.

A separate acute exposure and risk assessment was conducted for children to take account of their different physiological and behavioural parameters that can result in different exposures (e.g., hand-to-mouth exposures through touching treated turf). The endpoint of concern was increased incoordination and slight gait abnormalities noted in the acute neurotoxicity study in rats. In this study, the NOAEL was 75 mg/kg bw/day based on acute neurotoxic effects occurring at the LOAEL of 250 mg/kg bw/day. The target MOE was 300 based on application of the standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation), as well as an extra 3× safety factor to protect for potential sensitivity of the young noted in a series of published neurotoxicity studies. The skeletal variations identified in the rat developmental toxicity study above were not considered relevant to this subpopulation because this effect is a result of in utero exposure of a developing organism.

For short-term (1–7 day) dermal and inhalation exposures to 2,4-D acid, DMA, EHE or BEE, effects resulting from the oral route of exposure were used for risk assessment. This was because the 21-day dermal studies did not demonstrate any systemic toxicity, and the inhalation studies submitted were for acute exposure only. Again, the adult risk assessment was based on the most sensitive subpopulation, pregnant women. The maternal NOAEL of 30 mg/kg bw/day (2,4-D acid, DMA, EHE) or 10 mg/kg bw/day (2,4-D BEE), established in the respective rabbit developmental studies were selected, based on an increase in maternal deaths and morbidity at the LOAEL (90 mg/kg bw/day 2,4-D acid, DMA, EHE; 30 mg/kg bw/day 2,4-D BEE). In each case the target MOE was 1000, based on standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation) and an additional 10× safety factor to account for the severity of the maternal endpoint (morbidity and mortality). This target MOE is inherently protective of any uncertainty regarding potential sensitivity to the young.

To assess the risk to toddlers that could result from any potential non-dietary short-term oral exposure, oral developmental studies were considered most relevant with respect to route, duration of dosing and measurement of offspring sensitivity. The rat developmental study was chosen, which had a NOAEL of 12.5 mg/kg bw/day based on a decrease in body-weight gain at the LOAEL of 50 mg/kg bw/day. The target MOE was 300 based on application of the standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation) as well as an additional 3× safety factor as protection for potential sensitivity to the young, noted in a limited rat reproduction study and in a series of published neurotoxicity studies.

Since most animal toxicity studies involve exposure via the oral route, estimations of risk resulting from dermal exposure to humans must include a correction for the differences between oral and dermal absorption. A dermal absorption value of 10% was incorporated into the dermal estimates of exposure for all scenarios. This value is based on the weight of evidence from several published studies (Feldman and Maibach 1974; Harris and Solomon 1992; Moody et al. 1990; Wester et al. 1996; Pelletier et al. 1988), taking into consideration the variability in the data and the limitations of the various studies.

As stated in Section 4.1, the PMRA does not consider the DEA form of 2,4-D to be toxicologically equivalent to the other forms of 2,4-D. The registrant has submitted additional information regarding the toxicity of DEA to the PMRA for consideration. Mitigation measures for the DEA form of 2,4-D may be proposed depending on the outcome of the current review of this additional information. Therefore, a residential risk assessment for 2,4-D DEA has not been included at this time.

4.2.2 Exposure and risk assessment for homeowners mixing, loading and applying 2,4-D to residential lawns

Homeowners typically apply 2,4-D to their lawns twice a year, in the spring and fall, with occasional additional spot applications in the summer. Residential applicators, therefore, have the potential for short-term periods of exposure (less than 7 days). A separate acute (1-day) assessment was not required because the exposures would be the same as those considered in the short-term assessment.

Dermal and inhalation exposure estimates for homeowner application to residential turf are based on data from the Pesticide Handlers Exposure Database Version 1.1 (PHED), Outdoor Residential Exposure Task Force (ORETF) studies, and several published biomonitoring studies (Harris 1991; Harris and Solomon 1992; Solomon et al. 1992, 1993).

The PHED is a compilation of generic mixer/loader applicator passive dosimetry exposure data that can be used to generate scenario-specific exposure estimates. The ORETF studies monitored exposure to workers and homeowners mixing/loading and applying pest control products to turf. Monitoring was conducted using passive dosimetry, including hand washes, face/neck wipes and personal air samplers. Harris and Solomon (1991, 1992, 1993) measured total body exposure to homeowners applying 2,4-D by monitoring urinary excretion of 2,4-D. The study was conducted with two types of application equipment and two levels of personal protective equipment. Ninetieth percentile exposure estimates were used to estimate risk.

Exposure is calculated as the product of the unit exposure for a given scenario, the application rate and the area treated per day divided by body weight. For broadcast applications, it was assumed residential applicators treated 2000 m^2 a day. This is considered an upper percentile estimate.

Exposure and risk estimates and details on the calculations are presented in Appendix II. MOEs for residential applicators wearing only shorts and a short-sleeved shirt were above the target MOE of 1000 for short-term exposure at an application rate of 1.75 kg a.e./ha, with the exception of broadcast application to a large area with handheld equipment. The MOE was slightly below target for an individual wearing only shorts and a short-sleeved shirt, but MOEs were above target for an individual wearing long pants and a short-sleeved shirt treating a smaller area or using a lower application rate (1.25 kg a.e./ha).

There are no domestic class 2,4-D BEE formulations registered that could be mixed, loaded and applied by a homeowner.

4.2.3 Exposure and risk assessment for persons entering a treated area

Postapplication exposure and risk were estimated for children and adults contacting treated residential lawns and golf courses, based on assumptions outlined in the USEPA's draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments and the recommended revisions by the USEPA's Science Advisory Council (USEPA 1997b, 2001).

Postapplication dermal exposures were estimated using generic transfer coefficients and 2,4-D turf transferable residue (TTR) data. Transfer coefficients are defined in the EPA draft SOP and measure the relationship between dermal exposure and TTR for individuals engaged in a specific activity on treated turf.

Acute and short-term risk assessments were conducted as there is potential for relatively higher exposures to children and adults on the day of application, and for repeated lower exposures over a short-term period (1 to 7 days), as 2,4-D residues dissipate. Based on TTR data generated by the Broadleaf Turf Herbicide Transferable Foliar Residue task force, peak TTR levels were 2.63% of the applied rate and 7–day average TTR levels were 0.35% of the applied rate.

New postapplication exposure data relevant to estimating dermal exposure from contact with treated turf were received from the ORETF in February 2004. The PMRA, the USEPA and the California Department of Pesticide Regulation are currently evaluating these data. Preliminary calculations suggest that, while exposure estimates might increase slightly, target MOEs would still be met for all postapplication scenarios. If necessary, the PMRA will publish a revised risk assessment after a full review of the new data.

Non-dietary oral exposure was assessed for toddlers, as they could potentially ingest residues through hand-to-mouth transfer from turf or other surfaces, by mouthing grass or by ingesting soil. As well, oral ingestion of granules was considered, although this is considered to be an acute, episodic exposure event, rather than a typical exposure.

The contribution of inhalation exposure to overall exposure in postapplication scenarios is considered to be negligible, due to the low volatility of 2,4-D and the dilution effect of outdoor use. This rationale is supported by evidence from several published studies (Harris 1991; Harris and Solomon 1992; Solomon et al. 1992, 1993; Yeary and Leonard 1993; Nishoka et al. 1999; Whitmore et al. 1994).

The results of biomonitoring studies (Harris 1991; Harris and Solomon 1992; Solomon et al. 1992, 1993) were also considered in the risk assessment. Harris and Solomon (1991, 1992, 1993) monitored urinary excretion as a measure of exposure to 2,4-D following re-entry into turf treated by homeowners or professional applicators. Following either professional or homeowner application of 2,4-D, no 2,4-D residues were detected in urine samples from bystanders. During application, levels of 2,4-D were monitored in air samples both inside the home and outdoors, downwind of the application site. Residues

of 2,4-D were found in only 5 of the 76 air samples (2 indoor and 3 outdoor), with concentrations ranging from 2.2–20 µg of 2,4-D/m^3, and none was associated with detectable bystander exposure. Following professional application, air samples collected as described above contained no detectable 2,4-D residues. In a third study, the total body dose of 2,4-D was determined by monitoring urinary excretion in volunteers re-entering treated turf 1 hour and 24 hours after application. Transferable residues of 2,4-D sampled during the exposure sessions showed a rapid decline 24 hours following application. There were no detectable residues for individual wearing long pants, a short-sleeved shirt, socks and closed footwear re-entering treated turf at the 1-hour interval or for any individual re-entering treated turf 24 hours following application. Ninetieth percentile exposure values for people wearing shorts, t-shirts and no shoes were used in the risk assessment.

For all the calculation methods, all acute and short-term calculated MOEs for adults and toddlers exceeded the target MOEs for 2,4-D acid, DMA, EHE and BEE. This indicates that the potential exposures are below levels that would be of concern. Further details of calculations and exposure and risk estimates are presented in Appendix II.

4.3 Dietary assessment

A dietary exposure assessment was conducted so that aggregate exposure and risk could be estimated. An aggregate risk assessment considers the risk resulting from combined exposures from all sources and routes, including food, drinking water and residential exposures.

4.3.1 Dietary exposure

The dietary exposure assessment estimated how much 2,4-D residue, including residues in milk and meat, may be ingested with the daily diet. The assessment was age-specific and incorporated the different eating habits of the population at various stages of life. For example, the assessment took into account the greater consumption of fruit, vegetables and juices by children, relative to their body weight, compared to adults.

The assessment is based on the current definition that the residue of concern is 2,4-D, which is the parent compound (Canada Food and Drug Regulations, Division 15, Table II). All Canadian and American food commodities for which 2,4-D has a registered use were considered in the dietary risk assessment. Canadian uses for 2,4-D that could result in residues on foods and feeds include the following: alfalfa, apple, apricot, asparagus, barley, blueberry, cereals, cherry (including sweet and sour), clover, corn (including sweet), cranberry, flax, grasses (including forage, pasture, and rangeland), maple, millet, oyster beds, peach, pear, plum, raspberry, rye, sorghum, strawberry, wheat (including seed production, spring, winter, durum varieties) and water systems.

Data used to refine the dietary exposure estimates included surveillance data and processing studies, anticipated residues from animal metabolism studies, and the use of percent crop treated information for potentially treated imports from the United States. Where no data were available, potentially treated commodities were assessed using the default maximum residue limit (MRL) of 0.1 ppm under general regulation B.15.002(1) of the Food and Drug Regulations. The dietary exposure and risk estimates were generated using Dietary Exposure Evaluation Model (DEEM®) software and updated consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes of Individuals (1994–1998).

4.3.2 Dietary risk

An acute dietary exposure assessment considers the highest probable consumption of 2,4-D on any one day. A probabilistic statistical analysis allows all possible combinations of food consumption and residue levels to be combined to generate a distribution of the amount of 2,4-D residue that might be eaten in a day. A value representing the high end (99.9th percentile) of this distribution, which is referred to as the potential daily intake (PDI), is compared to the acute reference dose (ARfD). The ARfD is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake (PDI) from residues is less than the ARfD, this intake is not considered to be of concern.

In order to protect expectant mothers and unborn children, an ARfD was set at 0.08 mg/kg bw/day. This was based on the lowest rat developmental NOAEL of 25 mg/kg bw/day (a.e.) and application of a 300× uncertainty/safety factor (10× for interspecies variation, 10× for intraspecies variation and an additional 3× to account for potential sensitivity to the young noted in a series of published neurotoxicity studies). In this study, increased skeletal variations were noted at the LOAEL of 75 mg/kg bw/day. The acute PDI (99.9th percentile) for females of childbearing age accounted for less than 16.3% of the ARfD. The acute PDI for all other subpopulations was less than 9.9% of the ARfD (Table 4.3.2.1).

Chronic dietary exposure is calculated using the average consumption of different foods and average residue values on those foods over a 70-year lifetime. This expected intake of residues is compared to the acceptable daily intake (ADI), which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the expected intake from residues is less than the ADI, this intake is not considered to be of concern.

The ADI was set at 0.003 mg/kg bw/day. This ADI is based on a NOAEL of 1 mg/kg bw/day from long-term dietary studies in rats and applying a 300× uncertainty/safety factor. At the next highest dose level, kidney effects were noted. In addition to the standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation), an additional safety factor of 3× was applied for potential sensitivity to the young noted in a limited rat reproduction study and in a series of published neurotoxicity

studies. This provides margins of safety of 6000 to the NOAEL of 20 mg/kg bw/day in the rat reproduction study, where selective pup mortality was noted at 80 mg/kg bw/day, and 3000 to the NOAEL of 10 mg/kg bw/day for 2,4-D BEE where selective maternal mortality was noted in the rabbit developmental study. The chronic PDI accounted for less than 24% of the ADI for all population subgroups.

These chronic and acute dietary risk assessments demonstrated that there were no health concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors. The dietary exposure estimates are presented hereafter in Table 4.3.2.1.

Table 4.3.2.1 Chronic and acute dietary exposure and risk summary for 2,4-D

Population subgroup	Chronic dietary exposure		Acute dietary exposure	
	mg/kg bw/day	% ADI	mg/kg bw/day	% ARfD
General population	0.00031	10	0.0159	6.4
Infants/Children 1–6 years	0.00071	24	0.0247	9.9
Children/Youth 7–12 years	0.00038	13	0.0126	5
Females 13–50 years	0.00028	10	0.013	16.3

[1] Body weight is 70 kg for the general population, 62 kg for females, 39 for children/youth and 10 kg infants/children.

4.3.3 Drinking water

As indicated above, residues in drinking water can be a potential source of exposure to 2,4-D. To evaluate the contribution from this source to overall exposure, drinking water quality monitoring data from several sources, ranging from provincial reports to scientific studies, were considered. The combined Canadian data set incorporated monitoring results from ambient surface water and groundwater, as well as treated municipal drinking water. These data were supplemented by relevant monitoring information from the United States. Based on these data, the locations of high 2,4-D concentrations are generally randomized and do not persist. When detected, residues of 2,4-D in ambient and treated drinking were generally < 1 µg/L. The maximum estimates of acute and chronic residues of 2,4-D in drinking water were 50 and 0.3 µg/L, respectively.

studies. This provides margins of safety of 6000 to the NOAEL of 20 mg/kg bw/day in the rat reproduction study, where selective pup mortality was noted at 80 mg/kg bw/day, and 3000 to the NOAEL of 10 mg/kg bw/day for 2,4-D BEE where selective maternal mortality was noted in the rabbit developmental study. The chronic PDI accounted for less than 24% of the ADI for all population subgroups.

These chronic and acute dietary risk assessments demonstrated that there were no health concerns for any population subgroup in Canada, including infants, children, teenagers, adults and seniors. The dietary exposure estimates are presented hereafter in Table 4.3.2.1.

Table 4.3.2.1 Chronic and acute dietary exposure and risk summary for 2,4-D

Population subgroup	Chronic dietary exposure		Acute dietary exposure	
	mg/kg bw/day	% ADI	mg/kg bw/day	% ARfD
General population	0.00031	10	0.0159	6.4
Infants/Children 1–6 years	0.00071	24	0.0247	9.9
Children/Youth 7–12 years	0.00038	13	0.0126	5
Females 13–50 years	0.00028	10	0.013	16.3

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Canadian drinking water levels of comparison (DWLOCs) were calculated to assess whether these concentrations posed any risk. The DWLOC is the maximum concentration in drinking water which, when considered together with all other sources of exposure, does not exceed a level of concern. The acute and chronic DWLOC's were > 2077 and 23 µg/L, respectively. Since the acute and chronic anticipated residues of 2,4-D in drinking water do not exceed the respective DWLOC's indicated in Table 4.3.3.1, they are below the PMRA's level of concern.

Table 4.3.3.1 Chronic and acute drinking water levels of comparison for 2,4-D

Population subgroup	Short-term and chronic drinking water exposure	Acute drinking water exposure
	DWLOC[1] µg/L	DWLOC[1] µg/L
General Population	94	8194
Infants/Children 1–6 years	23	2253
Children/Youth 7–12 years	51	4629
Females 13–50 years	84	2077

[1] Where DWLOC = (reference dose - dietary exposure) × (body weight) ÷ (water consumption). Body weight is 70 kg for the general population, 62 kg for females, 39 for children youth and 10 kg infants/children. Water consumption is 2 L/day, except infants/children for whom water consumption is 1 L/day.

4.4 Aggregate risk assessment

The purpose of aggregating exposure is to estimate the risk resulting from total exposure to 2,4-D from all sources and routes of exposure, including food, drinking water and residential exposures.

4.4.1 Acute aggregate risk assessment

Acute aggregate risk is estimated as the risk that would result from the highest probable single day exposures to 2,4-D. Acute aggregate exposure to 2,4-D combines dietary and drinking water exposures only. The acute aggregate risk assessment did not incorporate residential exposure as it is improbable that an individual would be exposed to high-end dietary and residential exposures on the same day. Average (chronic) dietary exposure is a very small fraction of the highest one-day residential exposure and would not have an impact on the total risk.

The acute PDI (99.9th percentile) for females of childbearing age accounted for less than 16.3% of the ARfD. The acute PDI for all other subpopulations was less than 9.9% of the ARfD (Table 4.3.2.1).

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To aggregate the acute drinking water and dietary exposure, acute DWLOCs of greater than 2077 µg/L were calculated and assessed against the acute drinking water estimate of 50 µg/L. The acute exposure from drinking water sources is below the DWLOC. Since both the dietary and drinking water exposures are acceptable, the acute aggregate exposure is not of concern.

4.4.2 Short-term aggregate risk assessment

Short-term aggregate exposure to 2,4-D was estimated based on contributions from food, drinking water and residential exposure (dermal, inhalation and oral components).

With respect to route of exposure, there was no systemic toxicity in short-term dermal exposure studies. However, the oral route of exposure (rat and rabbit developmental studies) confirmed that decreases in body weight and/or body-weight gain were consistent endpoints of concern. Despite the absence of repeat-dose inhalation data, it was assumed that body weight effects would also be a critical endpoint by this route of exposure. Thus, the most relevant study to assess short-term aggregate exposure was the repeat-dose developmental toxicity study in rats, which established a NOAEL of 12.5 mg/kg bw/day based on decreased body weight gain. A target MOE of 300 was established for the general population, including children. This was based on standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation) and an additional 3× safety factor to account for potential sensitivity to the young noted in a limited rat reproduction study as well as in a series of published neurotoxicity studies.

For females of child-bearing age (females 13–50 years), an additional endpoint of concern for short-term aggregate exposure to both 2,4-D a.e and 2,4-D BEE was the observation of maternal toxicity (morbidity and mortality) in the oral rabbit developmental studies (NOAELs: 30 and 10 mg/kg bw/day; LOAELs: 90 and 30 mg/kg bw/day, respectively). It was assumed that this effect could manifest via either oral, dermal or inhalation routes of exposure. A target MOE of 1000 was established for this endpoint, which included standard uncertainty factors (10× for interspecies extrapolation, 10× for intraspecies variation) and an additional safety factor of 10× to account for the severity of the endpoint (morbidity/mortality). This target MOE is inherently protective of any uncertainty regarding potential sensitivity to the young.

The chronic dietary exposure was considered representative of a typical exposure, since it represents the average daily exposure over an individual's lifetime. Ingestion of granules is not aggregated in the short-term oral scenario as this is considered to be an episodic rather than a typical exposure event.

Dermal exposure was extrapolated to a systemic exposure by considering a 10% dermal absorption factor. Inhalation exposure and oral ingestion through dietary and non-dietary pathways are considered to be 100% absorbed. However, the contribution from inhalation exposure in postapplication scenarios is considered to be negligible, due to the low volatility of 2,4-D and the dilution effect of outdoor use patterns as well as supporting evidence in Harris (1991), Harris and Solomon (1992), Solomon et al. (1992, 1993), Yeary and Leonard (1993), Nishoka et al. (1999), and Whitmore et al. (1994).

Short-term aggregate exposure estimates from food, residential exposure (dermal, inhalation and incidental oral components) and drinking water did not indicate any unacceptable risk. The calculated DWLOCs ranged from 170 to 910 µg/L, with the most sensitive population subgroup being females 13–50 years re-entering areas treated with 2,4-D BEE. These were compared to the chronic estimate of 2,4-D residues in drinking water, which is 0.3 µg/L. This is lower than the calculated DWLOCs for all populations and, therefore, is below the PMRA's level of concern.

Further details of the exposure calculations and estimates of short-term aggregate exposure and risk are summarised in Appendix II.

4.4.3 Chronic aggregate risk assessment

Chronic aggregate exposure to 2,4-D is considered to arise from dietary and drinking water exposures only, and is compared to the ADI. Residential exposure is not included, as all the relevant time frames and exposure routes are considered in the short-term aggregate risk assessment. The derivation of the dietary and drinking water exposure estimates is described in tables 4.3.2.1 and 4.3.3.1.

The chronic PDI accounted for less than 24% of the ADI for all population subgroups, with children 1–6 years being the most highly exposed subpopulation.

Chronic DWLOCs of greater than 23 µg/L were calculated and assessed against the chronic drinking water estimate of 0.3 µg/L. The chronic exposure from drinking water sources is below the DWLOC. Since both the dietary and drinking water exposures are acceptable, the chronic aggregate exposure is not of concern.

4.5 Occupational risk assessment

Occupational risk is estimated by comparing the potential exposure of persons mixing, loading and applying pesticides or re-entering treated areas, to the no-effect level for an endpoint from the most relevant toxicology study with respect to route and duration. This generates a MOE. The MOE is compared to a target MOE that incorporates safety factors protective of the most sensitive population. If the MOE is less than this target MOE, it does not necessarily mean that exposure will result in adverse effects, rather that the absence of adverse effects is less certain. Mitigation measures will be necessary to reduce exposure if MOEs are less than the target MOE.

4.5.1 Relevant toxicological endpoints and target margins of exposure for acute and short-term exposures to commercial applicators and re-entry workers

To protect the most sensitive subpopulation, the unborn child of pregnant workers (females 13–50 years), the most relevant endpoint for acute worker risk assessments was considered to be increased skeletal variations in rat fetuses noted in a rat developmental study. Protection of the most sensitive subpopulation is inherently protective of the general population. In this study, the NOAEL was 25 mg/kg bw/day a.e. based on increased skeletal variations in rat fetuses noted at the LOAEL of 75 mg/kg bw/day, an endpoint that could potentially occur following a single exposure event. The target MOE was 300 based on standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation) as well as an extra 3× safety factor to protect for potential sensitivity to the young noted in a series of published neurotoxicity studies.

For short-term dermal and inhalation exposures (1–7 days or 8–30 days) to 2,4-D acid, DMA, EHE or 2,4-D BEE, oral endpoints were selected that account for potential increased sensitivity to the neonate and pregnant women (females 13–50 years). Oral endpoints were used because the 21-day dermal studies did not demonstrate any systemic toxicity and the inhalation studies submitted were for acute exposure only. For females 13–50 years, NOAELs of 30 mg/kg bw/day (2,4-D acid, DMA, EHE) and 10 mg/kg bw/day (2,4-D BEE), established in rabbit developmental studies were used, based on increases in maternal deaths and morbidity at the LOAELs of 90 mg/kg bw/day and 30 mg/kg bw/day, respectively. An MOE of 1000 was selected based on the standard uncertainty factors (10× for interspecies variation, 10× for intraspecies variation), with an additional 10× to account for the severity of the maternal endpoint (death/morbidity). This target MOE is inherently protective of any uncertainty regarding potential sensitivity to the young, including the unborn child of a pregnant worker.

As oral toxicity endpoints were used, a dermal absorption value of 10% was incorporated into the dermal estimates of exposure for all scenarios (refer to Section 4.2.1).

As stated in Section 4.1, the PMRA does not consider the DEA form of 2,4-D to be toxicologically equivalent to the other forms of 2,4-D. The registrant has submitted additional information regarding the toxicity of DEA to the PMRA for consideration. Mitigation measures for the DEA form of 2,4-D may be proposed depending on the outcome of the current review of this additional information. Therefore, an occupational risk assessment for 2,4-D DEA has not been included at this time.

4.5.2 Exposure and risk assessment for commercial applicators mixing, loading and applying 2,4-D to residential lawns, golf courses and sod farm turf

Commercial lawn care operators treating residential lawns may be handling 2,4-D for one month during the spring and fall. Applicators treating golf course and sod farm turf are restricted to two applications per year and are likely to be exposed to 2,4-D for less than one week in the spring and fall.

Exposure estimates for mixer/loader/applicators were based on data from the PHED Version 1.1, ORETF studies and several published studies (Yeary 1986; Harris 1991; Solomon et al. 1992; Solomon et al. 1993; Yeary and Leonard 1993; Nishoka et al. 1999; and Whitmore et al. 1994). Refer to Section 4.2.2 for descriptions of the PHED data and ORETF studies.

Yeary (1986) measured urinary excretion of 2,4-D in commercial lawn specialists who had been spraying lawns on a daily basis for a period of at least three weeks. Average exposure data was used qualitatively in this assessment. Harris and Solomon (1991, 1992, 1993) conducted a series of biomonitoring studies in Ontario, Canada, assessing exposure associated with 2,4-D turf uses. A total dose of 2,4-D in professional applicators treating residential turf was measured by monitoring urinary excretion. The 90th percentile exposure values were used quantitatively in this risk assessment.

Exposure is calculated as the product of the unit exposure for a given scenario, the application rate and the area treated per day divided by the body weight. MOEs for commercial lawn care operators wearing pants, a long-sleeved shirt and gloves exceeded the short-term (8–30 day) target MOE. MOEs for commercial mixer, loader, applicators working on golf course and sod farms who wore long pants, a long-sleeved shirt and gloves are above the short-term (1–7 day) target MOE of 1000. Further details of the calculations and exposure and risk estimates are presented in Appendix II.

4.5.3 Postapplication exposure and risk assessment

Golf course and sod farm workers who re-enter treated sites to conduct turf maintenance activities may have acute and short-term (< 1 week) exposure to 2,4-D. Potential exposure was estimated using generic agricultural transfer coefficients (TC) for workers aerating, fertilizing, mowing, harvesting and transplanting treated turf, coupled with TTR data. A peak residue level of 2.63% of the applied rate was used for the acute risk assessment, and a 7-day average of 0.35% was calculated for the short-term risk assessment (1–7 days).

The MOEs for all golf course and sod farm postapplication activities are above the target MOEs for acute (1 day) and short-term (1–7 days) exposure.

5.0 Environmental assessment

Environmental risks from the use of 2,4-D on lawns and turf were assessed. The standard deterministic approach (tier 1) was used, and risk was characterized by the quotient method, the ratio of the estimated environmental concentration to the effects endpoint of concern for the most sensitive species.

Risk quotient values less than one are considered indicative of a low risk of non-target effects occurring, whereas values greater than one are considered to indicate that some degree of risk exists for effects on non-target organisms.

Initial and cumulative expected environmental concentrations (EECs) were calculated for soil and wildlife food sources for the spray formulations of 2,4-D used on lawn and turf by both commercial applicators and homeowners. Maximum and minimum application rates were used to calculate the EECs along with the maximum number of applications and minimum interval between applications.

5.1 Environmental fate

The solubility of 2,4-D varies considerably with the chemical form. The acid (23 g/L) and the dimethylamine salt (2,4-D DMA) (729 g/L) are very soluable in water. The ethylhexyl ester (2,4-D EHE) is insoluble (0.09 mg/L) but it rapidly transforms to the acid (WHO 1998). Their adsorption characteristics ($K_{OC} < 150$) also indicate that they are not adsorbed by soil (WHO 1998). Therefore, all of these forms are considered to be highly mobile and susceptible to run off from the treatment site. There may be a potential for leaching to groundwater, particularly in areas where the soils are permeable (e.g., sandy soil) and where the depth to the water table is shallow, provided there is rainfall soon after application.

2,4-D acid and the amines are non volatile owing to their low vapour pressures (WHO 1998). 2,4-D EHE and 2,4-D BEE esters are more volatile than the amines or the acid owing to their higher vapour pressure. Monitoring data indicate that 2,4-D is prevalent in prairie rainfall at low concentrations (Donald et al. 2001; Hill et al. 1999; Waite et al. 2002). However, this probably originates mainly with agricultural uses rather than turf and lawn uses, and will be addressed in the re-evaluation of 2,4-D agricultural uses.

Hydrolysis is not an important route of transformation for 2,4-D acid but is important for the esters in alkaline conditions (United Kingdom 1993). Phototransformation of 2,4-D acid is important in water but not in soil. The other chemical forms of 2,4-D are not affected by phototransformation in water or in soil. Aerobic biotransformation is the major route of transformation of 2,4-D as well as its amine and ester forms in soil and the aquatic environment. 2,4-D acid is classified as non-persistent to slightly persistent in soil and natural water because of aerobic biotransformation, with half-lives of 1.7 to 31 days in soil and 4.5 to 29 days in water. Biotransformation of the EHE and BEE esters in soil and natural water occurs rapidly with half-lives of less than two hours (WHO 1998). The biotransformation rate is reduced under anaerobic conditions, and the amine form (DMA) is persistent under anaerobic conditions with a half-life exceeding one year in sediments.

5.2 Environmental toxicology

2,4-D has low toxicity to honey bees, with a median lethal dose (LD_{50}) of more than 100 µg 2,4-D DMA/bee, and to earthworms, with a median lethal concentration (LC_{50}) of 350 mg 2,4-D DMA/kg soil (WHO/FAO 1997). The acute oral toxicity of 2,4-D for birds such as the mallard and the bobwhite quail ranges from slightly to moderately toxic. In acute oral tests, 2,4-D is slightly to moderately toxic to mammals. 2,4-D toxicity to fish varies from practically non-toxic to slightly toxic and to aquatic invertebrates, from practically non-toxic to moderately toxic depending upon the species.

2,4-D, being a herbicide, is toxic to many non-target terrestrial plants. The most sensitive species in the seed germination and emergence tests with the various forms of 2,4-D was the radish. For vegetative vigour, the most sensitive species to 2,4-D was the tomato. Freshwater aquatic macrophytes and algae are also sensitive to 2,4-D. For 2,4-D DMA, the 14-day no observed effect concentration (NOEC) for duckweed, *Lemna gibba*, is 0.27 mg 2,4-D DMA/L and the 5day NOEC for the alga, *Selenastrum capricornutum*, is 19.2 mg 2,4-D DMA/L.

5.3 Environmental risk assessments

5.3.1 Assessment of risks to terrestrial organisms

The risk to terrestrial invertebrates was determined to be low, as indicated by the low acute toxicity in the honey bee and earthworms.

For liquid formulations of 2,4-D, there is little or no risk of acute or reproductive effects to larger birds such as the mallard and the bobwhite. For smaller bird species such as the American robin and the sparrow, 2,4-D presents only a slight increase in the level of risk compared to larger birds. However, because of their diet, the actual exposure to 2,4-D is limited and the risk is much reduced.

The risk of 2,4-D when used in granular products was also assessed. Granular formulations provide a unique exposure scenario, because birds use grit to aid in digestion of food. The number of granules required to reach the LD_{50} for a particular size of bird and the number of granules available per metre square were compared to determine risk. For the granular products of 2,4-D, the assessment indicated some potential risk of acute effects to very small birds (sparrow size, less than 15 g), assuming the birds will consume the granules. However, the risk to small birds from granular formulations is limited because the granulars are much larger than their preferred grit size.

Based on acute oral toxicity, small mammals feeding on vegetation contaminated with 2,4-D are unlikely to be at risk. Based on reproductive toxicity, the potential risk to mammals from application of liquid formulations was determined to be moderate, except at the highest application rates (exceeding 1.75 kg 2,4-D/ha), where the potential risk of reproductive effects (decreased pup survival) was determined to be high. However, this may be an overestimate as the half-life of 2,4-D on plants is only about three days. For granular formulations, there was no significant risk to small mammals.

Using the toxicity data for terrestrial plants, and the minimum and maximum applications for 2,4-D, risk quotients ranged from 10 to 132 for seedling emergence and from 27 to 202 for vegetative vigour. These values indicate high risk to very high risk to non-target terrestrial plants from 2,4-D and its various forms.

5.3.2 Assessment of risks to aquatic organisms

For the assessment of risk to aquatic organisms, the potential exposures were estimated for non-residential areas (golf courses) where boom sprayers are used and for residential lawns where handheld sprayers are used.

For areas where boom sprayers are used, the EECs were based on maximum deposit that would result from accidental overspraying of a 1-ha pond of 30 cm depth at label rates.

For residential uses, the exposure scenario for aquatic systems was based on surface water monitoring data from urban areas in Ontario and Alberta. For the purpose of the risk assessment the maximum concentration detected was used.

The risk from acute toxicity of 2,4-D (as acid or DMA) to freshwater and marine/estuarine invertebrates and fish varied from no risk to low risk, even when a 100% deposit from spray drift was assumed. Based on laboratory tests, 2,4-D as EHE or BEE could potentially pose a moderate to high acute and chronic risk to freshwater invertebrates. However, in a real life situation the risk would be less than predicted because in natural water, biotransformation of the esters to the acid occurs rapidly (i.e., in less than two hours). This was supported by monitoring data showing that 2,4-D in runoff presents little or no potential risk to freshwater and estuarine/marine fish. Monitoring data also confirmed that there was no risk to aquatic invertebrates, except from the ester form (EHE). The EHE form presents a moderate risk owing to its higher toxicity than the other forms.

The potential risk to aquatic plants varied from low, from 2,4-D acid, to moderate, from the DMA, EHE and BEE forms of 2,4-D. The actual risk will also be similar to the acid for these other forms of 2,4-D, because they transform rapidly to the acid in natural water. The risk to algae and vascular aquatic plants from 2,4-D forms in runoff was low.

5.3.3 Environmental risk assessment conclusions

The environmental assessment shows that 2,4-D and equivalents when used on lawns and turf by homeowners and by professional applicators does pose a risk to terrestrial broadleaf non-target plants. This risk is not unexpected for a broad spectrum herbicide. Preventing spray from drifting into non-target areas offers a practical means to minimize the potential for adverse effects.

5.4 Potential for environmental risk mitigation

Spray drift can be mitigated through the use of spray buffer zones, or a combination of buffer zones and low-drift application technologies. Buffer zones prevent spray drift into non-target habitats, both terrestrial and aquatic. The assessment of 2,4-D for control of weeds on golf course turf indicated that buffer zones are not required for protection of aquatic habitats if 2,4-D is applied alone. However, if 2,4-D is applied with other herbicides, the more restrictive buffer zones apply, including any buffer zones for aquatic habitats (refer to Section 8.2.2).

The model used to determine buffer zones for turf use was based on spray drift studies that were conducted with boom sprayers. Since terrestrial non-target broadleaf plants are highly susceptible to 2,4-D spray drift, it is important that the applicator takes care not to directly spray, allow spray to drift onto or allow runoff to reach the roots of desirable non-target plants, including ornamentals.

2,4-D applied to areas that would require tractor pulled boom sprayers (or similar technologies) must comply with the buffer zones indicated on the label to protect non-target terrestrial plants (see Section 8.2.2). If the spray booms are equipped with shrouds or cones, the buffer zones presented in Section 8.2.2 can be reduced by 70% when shrouds are used and by 30% when cones are used.

6.0 Value

As indicated previously in Section 2.5, the re-evaluation of the lawn and turf uses of 2,4-D has focussed on the assessment of fine turf (i.e., sports and recreational turf, lawn turf and sod). Utility, or rough turf, is not included in this assessment.

2,4-D is a member of a group of chemicals that mimic the natural plant hormone indole-3-acetic acid (also known as auxin). When applied at appropriate rates, these herbicides produce an "auxin overload", thereby causing susceptible plants to be injured/controlled.

Commercial products are applied postemergence (once weeds have already germinated) with groundboom, backpack and handheld sprayers; low-pressure lawn spray guns; or spreaders. Domestic products are generally applied with backpack or handheld sprayers, sprayers attached at the end of a watering hose or ready-to-use applicators (e.g., bottle sprayers or wipe applicators). Spreaders are generally used for broadcast and spot treatment with granular fertilizer/herbicide combination products.

In a 1988 report commissioned by Agriculture and Agri-Food Canada, it was estimated that 342 000 kg of 2,4-D a.e. were used for broadleaf weed control on turf in Canada per year. This represented 7% of the total estimated 2,4-D use in Canada at that time. Since the publication of that report, the total 2,4-D consumption in Canada is estimated to have decreased by 30%. The decrease in total 2,4-D use was due to the recent registration of alternatives to 2,4-D for agricultural uses.

A total of 69 products (37 commercial and 32 domestic class products) containing 2,4-D are registered under the *Pest Control Products Act* for use on fine turf in Canada, including 35 coformulations of 2,4-D, mecoprop and dicamba; 10 coformulations of 2,4-D and mecoprop; 1 coformulation of 2,4-D and dicamba; and 23 products that contain only 2,4-D (as of 12 February 2004). All products are applied as sprays, except for two domestic class products that are solid formulations (bar and stick).

In addition to these products, there are numerous fertilizer/herbicide products registered for use on fine turf in Canada that contain 2,4-D. These fertilizer/herbicide products are registered with the Canadian Food Inspection Agency under the *Fertilizers Act* and not with the PMRA under the *Pest Control Products Act*. However, the conditions for use of these products must reflect the registered uses for the pesticide under the *Pest Control Products Act*.

The majority of products contain either 2,4-D, mecoprop and dicamba, or 2,4-D and mecoprop. Although these three herbicides are all broadleaf herbicides, the weed control spectra and the efficacy for certain broadleaf weeds of mecoprop and dicamba are different from 2,4-D and, therefore, they are used in combination with it to broaden the weed control spectrum of herbicide and herbicide/fertilizer products. It is best to think of 2,4-D as the main ingredient in these coformulations, and of mecoprop and dicamba as supplements used to improve efficacy on certain weeds. Mecoprop and dicamba alone are not as effective for broadleaf weed control on turf as when they are used in combination with 2,4-D. Combinations of 2,4-D, mecoprop and dicamba, especially at a ratio of 2:1:0.1, have been shown to be synergistic; therefore, if mecoprop and dicamba were used separately but in sequence, the rate required to obtain a similar level of weed control would be significantly higher than the rate used in coformulations. As such, coformulated products at a ratio of 2:1:0.1 2,4-D/mecoprop/dicamba represent the least amount of individual active ingredient for any given level of efficacy.

With respect to weed control spectrum, there is no real benefit in replacing 2,4-D with another phenoxy herbicide like MCPA [(4-chloro-2-methylphenoxy) acetic acid, CAS chemical name], by virtue of the fact that their properties are so similar. Aside from MCPA, which is not coformulated with 2,4-D, no domestic or commercial class herbicide that has a weed control spectrum equivalent to 2,4-D is currently registered in Canada for use on fine turf.

Over the past 40 years, 2,4-D has played an important role in the maintenance of turf. Without it, the number of broadleaf weed control products presently available to homeowners would be severely limited. According to the PMRA database, very few domestic class products that do not contain 2,4-D are registered for use on lawns to control broadleaf weeds.

The PMRA announced the launch of a label improvement program for all 2,4-D products in 1994. At that time, the maximum label rate for turf was adjusted to 2.24 kg a.e./ha under the PMRA's efforts to harmonize rates with the USEPA. A review of the recommendations for the application rates for turf and lawn on the labels of currently registered products containing 2,4-D indicated that the minimum effective rate is lower than the current maximum of 2.24 kg a.e./ha.

The Industry Task Force II on 2,4-D Research Data supports an overall rate reduction from 2.24 to 1.75 kg a.e./ha for all applications to turf including granular and liquid formulations.

Solid formulations
For granular products (2,4-D alone or coformulated and impregnated on granules, including fertilizer granules) and solid (bar and stick) formulations, the PMRA accepts the Task Force's proposition of 1.75 kg a.e./ha as the maximum rate of 2,4-D.

Liquid formulations
For liquid products containing 2,4-D alone, the PMRA proposes to reduce the maximum 2,4-D rate for turf to 1.55 kg a.e./ha for the following reasons:

1. Based on the available information, liquid formulations are consistently more effective than granular formulations at the same rate.

2. All currently registered domestic class products already have a maximum rate lower than 1.55 kg a.e. 2,4-D/ha.

3. Most commercial class products have a maximum rate equal to or lower than 1.55 kg a.e. 2,4-D/ha; only 3 out of 18 products have a rate greater than 1.55 kg a.e. 2,4-D/ha. Those three products also have a range of rates that start under 1.55 kg a.e. 2,4-D/ha.

For liquid coformulated products (two-way and three-way), the PMRA proposes to reduce the maximum 2,4-D rate for turf to 1.25 kg a.e./ha for the following reasons:

1. Based on the available information, liquid formulations are consistently more effective than granular formulations at the same rate.

2. All currently registered coformulated commercial class products already have a maximum rate equal to or lower than 1.25 kg a.e. of 2,4-D/ha.

3. Most coformulated domestic class products also have a maximum rate equal to or lower than 1.25 kg a.e. of 2,4-D/ha; only 3 out of 29 products have a rate greater than 1.25 kg a.e. 2,4-D/ha.

With maximum application rates of 1.75, 1.55 and 1.25 kg a.e. of 2,4-D/ha for granular and solid formulations (2,4 D alone or coformulated), liquid single formulations and liquid coformulations respectively, 2,4-D products are efficacious.

2,4-D is efficacious against certain problematic broadleaf weeds on turf and there are no alternative herbicides to phenoxyalkanoic and benzoic acid herbicides on turf. Considering that weed control on turf is important, it is concluded that 2,4-D on turf has value.

7.0 Other assessment considerations

7.1 Toxic Substances Management Policy

During this review of the lawn and turf uses of 2,4-D the PMRA took into account the federal Toxic Substances Management Policy[6] and followed its Regulatory Directive DIR99-03[7]. The 2,4-D TGAI and its major transformation products do not meet the criteria for TSMP Track 1 substances.

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6 The federal Toxic Substances Management Policy is available through Environment Canada's website at www.ec.gc.ca/toxics

7 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, is available through the Pest Management Information Service. Phone: 1 800 267-6315 within Canada or (613) 736-3799 outside Canada (long distance charges apply); Fax: (613) 736-3758; E-mail: pmra_infoserv@hc-sc.gc.ca; or through our website at www.pmra-arla.gc.ca

The log *n*-octanol–water partition coefficient (log K_{ow}) for 2,4-D acid is less than 2.0, which is below the TSMP Track 1 cut-off criterion of log K_{ow} 5.0. The only form of 2,4-D that exceeds one of the TSMP Track 1 criteria is 2,4-D EHE, as it has a log K_{ow} of 5.8. However, 2,4-D EHE does not meet the persistence criterion. Esters such as EHE undergo rapid biotransformation (half-life of less than half a day) in natural water and soil; hence, their persistence is much less than the TSMP Track 1 cut-off criteria for water, sediment and soil (182 days in each medium).

7.2 Impurities, byproducts and contaminants

Based on the raw materials used for the manufacture of the 2,4-D technical products and the available chemistry data, it is not expected that 2,4-D would be contaminated with 2,3,7,8-TCDD or 2,3,7,8-substituted higher congeners. It is unlikely that these microcontaminants will be detectable in 2,4-D formulated products or in storm water runoff from treated fields. However, to reconfirm that these products continue to be free of TSMP Track 1 substances, the PMRA is requiring the submission of confirmatory data consisting of five recent batches of all technical products in order to validate absence of 2,3,7,8-TCDD, 2,3,7,8-TCDF and their respective higher substituted chlorinated congeners to the LOQs (see Section 9.1, Data Requirements relating to chemistry).

7.3 Formulant issues

Formulant issues are being addressed through the PMRA's Formulants Program, as outlined in the Regulatory Directive DIR2004-01.

Based on the considerations outlined in Section 4.1 (Toxicology summary), mitigation measures for the DEA form of 2,4-D may be proposed depending on the outcome of the current review of additional information.

DMA formulations may contain trace levels of N-nitrosodimethylamine (NDMA). Typically, NDMA, if present as a microcontaminant, is at a concentration of less than 1 ppm. Toxicology studies done with these pesticide formulations do not exhibit any of the toxicological findings that are characteristic of NDMA. Also, NDMA is rapidly decomposed by sunlight and, therefore, does not persist in the environment under use conditions. Thus, it is unlikely that trace levels of NDMA from pesticide sources would pose a health risk to humans. However, the PMRA will monitor the level of NDMA in certain formulations by requiring registrants to specify NDMA levels in the DMA used for manufacturing purposes (see Section 9.1.2).

8.0 Proposed regulatory actions

The use of 2,4-D on residential, recreational and commercial turf is acceptable for continuing registration. The addition of buffer zones to commercial products applied by tractor-pulled sprayers is required to protect surrounding broadleaf vegetation (see Section 8.1). Standard label precautionary statements and improvements are required, as described in Section 8.2.

8.1 Mitigation measure

Buffer zones required to protect terrestrial habitat, as shown in Section 8.2.3.

8.2 Label recommendations and improvements

8.2.1 General

The statement "Keep out of reach of children" must appear on the primary panel of all labels.

The following statement must appear under the "DIRECTIONS FOR USE" section of the label of commercial class products only:

- Do not apply by air.

The following statement must appear under the "DIRECTIONS FOR USE" section of the label of products intended for broadcast application:

- Do not apply more than two broadcast applications per season. This does not include spot treatments.

8.2.2 Label statements relating to health

The label text of **Commercial Class** products containing 2,4-D must include the following text:

Toxicological Information

2,4-D may cause severe irritation to the eyes. Prolonged breathing of 2,4-D may cause coughing, burning, dizziness or temporary loss of muscle coordination. Other possible effects include fatigue, muscle weakness or nausea. Treat symptomatically.

8.2.3 Label statements relating to the environment

The labels of all products must be amended to include the following statements:

ENVIRONMENTAL HAZARDS

- Toxic to terrestrial plants. This product will harm other broad leaved plants in the vicinity of the treatment area. If applying this product using a handheld sprayer, do not directly spray or allow the spray to drift onto ornamentals or gardens.
- Do not spray exposed roots of trees and ornamentals.
- Do not contaminate irrigation / drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
- Avoid application when heavy rain is forecast.
- To reduce runoff from treated areas into aquatic habitats, consider the characteristics/conditions of the site before treatment. Site characteristics/conditions that may lead to runoff include, but are not limited to heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g., soils that are compacted, fine textured or low in organic matter). Potential for contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body. To prevent runoff avoid spraying on driveways, sidewalks or any other hard surface. Do not irrigate within 24 hours after application.
- The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g., sandy soil) and/or the depth to the water table is shallow.

In addition, the labels of liquid commercial class products that may be applied by tractor-pulled field sprayers (e.g., to golf courses or sod farms) must include the following statements:

Buffer Zones

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as non-target grasslands, forested areas, shelter belts, woodlots, hedgerows, pastures, rangelands, and shrublands).

- Do not apply during periods of dead calm or when winds are gusty.

- When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

- **Buffer zones**

Buffer zones (metres) required to protect terrestrial habitat when using tractor-pulled boom sprayers	
2,4-D derivative	**Label buffer zone**
Acid	30
DMA	20
EHE	30
BEE	20

Buffer zones can be reduced 70 % when using shrouds or 30% when using cones.

8.2.4 Label statements related to value

For consistency, maximum application rates on all labels for turf use are limited to the following:

- 1.75 kg a.e. 2,4-D/ha for solid products containing 2,4-D alone or coformulated (granules, bar and stick);
- 1.55 kg a.e. 2,4-D/ha for liquid products containing 2,4-D alone; and
- 1.25 kg a.e. 2,4-D/ha for liquid products containing 2,4-D coformulated with other active ingredients (two-way and three-way mixtures).

The following statements are to be included in the Directions for Use section of the label, under the claim, of all products containing 2,4-D applied to turf:

- Efficacy is best when a herbicide is applied to actively growing weeds

The following statements are to be included in the Directions for Use section of the label, under the application directions, of all products containing 2,4-D applied to turf by broadcast application:

- If weed populations do not warrant a broadcast application (e.g., entire lawn) consider spot treatments that target only weedy areas.

- When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

- **Buffer zones**

Buffer zones (metres) required to protect terrestrial habitat when using tractor-pulled boom sprayers	
2,4-D derivative	**Label buffer zone**
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- Efficacy is best when a herbicide is applied to actively growing weeds.

The following statements are to be included in the Directions for Use section of the label, under the application directions, of all products containing 2,4-D applied to turf by broadcast application:

- If weed populations do not warrant a broadcast application (e.g., entire lawn) consider spot treatments that target only weedy areas.

9.0 Additional data requirements

9.1 Data requirements relating to chemistry

9.1.1 Technical grade active ingredient

To update the chemistry database and to convert the guarantee of 2,4-D in the technical grade products from a minimum to a nominal value, the following data are required.

Table 9.1.1.1 Chemistry data requirements

Registration number	Required chemistry data—Data codes (DACOs)
17134	Complete DACO title 2 data. The chemistry data were previously submitted in from 1984 to 1986.
17045	Complete DACO title 2 data. The chemistry data were previously submitted in 1987.

To reconfirm that the products continue to be free of TSMP Track 1 substances, five recent batches of all technical products are required to analyse for 2,3,7,8-TCDD, 2,3,7,8-TCDF and their respective higher substituted chlorinated congeners to the LOQs, as established by members of the Industry Task Force II on 2,4-D Research Data and supported by validation data.

9.1.2 All products to which DMA is added during the manufacturing/formulation process

An updated Statement of Product Specification form is required for all products to which DMA is added during the manufacturing/formulation process. The form must identify the levels of NDMA present in the DMA that is used. This requirement pertains only to products where DMA is added as part of the manufacturing/formulating process; it does not apply to products that utilize the already manufactured DMA form of 2,4-D in the formulation process.

9.2 Data requirements relating to toxicology

The PMRA has accounted for uncertainties associated with some studies considered in the risk assessment through safety factors. The following confirmatory data are required to refine the risk assessment:

- A developmental neurotoxicity study using 2,4-D acid, complete with adequate histopathological examination of myelin deposition (DACO 4.5.14). This data requirement is based on evidence of neurotoxicity in guideline and published studies.

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An updated Statement of Product Specification form is required for all products to which DMA is added during the manufacturing/formulation process. The form must identify the levels of NDMA present in the DMA that is used. This requirement pertains only to products where DMA is added as part of the manufacturing/formulating process; it does not apply to products that utilize the already manufactured DMA form of 2,4-D in the formulation process.

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The PMRA has accounted for uncertainties associated with some studies considered in the risk assessment through safety factors. The following confirmatory data are required to refine the risk assessment:

- A developmental neurotoxicity study using 2,4-D acid, complete with adequate histopathological examination of myelin deposition (DACO 4.5.14). This data requirement is based on evidence of neurotoxicity in guideline and published studies.

- A multigeneration reproduction study using 2,4-D acid (DACO 4.5.1). Limitations in the existing reproduction study preclude a detailed assessment of potential sensitivity to the young.

9.3 Data requirements relating to occupational and bystander exposure

All registrants must either gain access to data of the Broadleaf Turf Herbicide Task Force and the ORETF, or provide equivalent data.

10.0 Proposed re-evaluation decision

The PMRA has carried out an assessment of the available information and has concluded that the use of 2,4-D and associated EPs to treat lawns and turf does not entail an unacceptable risk of harm to human health or the environment, provided the mitigation measure recommended in this document is adopted. Standard precautionary statements and label improvements are also recommended.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed decision.

List of abbreviations

ADI	acceptable daily intake
a.e.	acid equivalent
a.i.	active ingredient
ARfD	acute reference dose
BEE	butoxyethyl ester
bw	body weight
CML	canine malignant lymphoma
DACO	data code
DEA	diethanolamine
DEEM®	Dietary Exposure Evaluation Model
DFR	dislodgeable foliar residue
DMA	dimethylamine
DWLOC	drinking water level of comparison
EC	European Commission (also known as European Union)
EEC	expected environmental concentration
EHE	ethylhexyl ester
F1	first filial generation
F2	second filial generation
FAO	Food and Agriculture Organization of the United Nations
ha	hectare
IR	ingestion rate
JMPR	Joint WHO/FAO Meeting on Pesticide Residues
kg	kilogram
K_{oc}	absorption quotient normalized for organic carbon
K_{ow}	*n*-octanol–water partition coefficient
LOAEL	lowest observed adverse effect level
LC_{50}	mean lethal concentration
LD_{50}	mean lethal dose
LOQ	level of quantitation
m	metre
MCPA	(4-chloro-2-methylphenoxy) acetic acid (CAS name)
mg	milligram
MOE	margin of exposure
MRL	maximum residue limit
n/a	not applicable
NDMA	N-nitrosodimethylamine
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
ORETF	Occupational and Residential Exposure Task Force
Pa	Pascal
PDI	potential daily intake
PHED	Pesticide Handlers' Exposure Database
PMRA	Pest Management Regulatory Agency
ppb	parts per billion

ppm	parts per million
RED	Reregistration Eligibility Document
REI	restricted entry interval
ROC	residue of concern
RQ	risk quotient
SA	surface area
SEF	saliva extraction factor
TC	transfer coefficient
TTR	turf transferable residue
TSMP	Toxic Substances Management Policy
U.K.	United Kingdom
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency
WHO	World Health Organization

Appendix I Key elements of the 2,4-D Science Advisory Panel report

In June 2003, the PMRA convened an independent five-member expert Science Advisory Panel for the purpose of providing input into the mammalian toxicology and exposure re-evaluations, the preliminary human health risk assessment as well as the environmental risk assessment of 2,4-D for lawn and turf use. The Panel members included Dr. Tye Arbuckle, Healthy Environments and Consumer Safety Branch, Health Canada; Mr. Jeff Dawson, USEPA; Dr. Claire Infante-Rivard, Department of Epidemiology, Biostatistics and Occupational Health, McGill University; Dr. Leonard Ritter, Canadian Network of Toxicology Centres and Department of Environmental Biology, University of Guelph (Panel Chairperson); and Dr. Keith Solomon, Centre for Toxicology and Department of Environmental Biology, University of Guelph.

Panel members were provided with the draft PMRA assessment prior to their meeting, where the assessments were presented and discussed. Subsequent to the meeting, additional supporting data and information were provided to Panel members, as requested, and the 2,4-D Science Advisory Panel submitted a final report to the PMRA in January 2004. Panel comments were carefully considered by the PMRA and reflected as appropriate in this document. Below is a summation of the key comments from the Panel's report.

Overall, the 2,4-D Science Advisory Panel concurred with the general thrust of the PMRA evaluation. The Panel endorsed the following positions held by the PMRA.

- Various forms of 2,4-D share the same toxicological profile, with the exception of 2,4-D DEA. The Panel noted that additional data would be needed prior to conducting a hazard or risk assessment for this form.

- The Panel supported the PMRA's request for additional studies to address uncertainties relating to potential reproductive and developmental neurotoxicity.

- The Panel concurred with applying an additional three-fold safety factor to address uncertainties regarding possible increased sensitivity of the young.

- The Panel supported applying an additional safety factor to address severe maternal toxicity. The Panel indicated that no adjustments to the uncertainty factors proposed by the PMRA were necessary.

- The Panel agreed with the PMRA's conclusion that the toxicological database does not suggest a carcinogenic risk. However, the Panel was unable to reach a conclusion on the classification of human carcinogenicity of 2,4-D. The Panel did note that the recent assessments carried out by the USEPA (1997a) and the European Commission (2001), as well as an independent carcinogenicity assessment (Gandhi et al. 2000), concluded that the overall human carcinogenicity of 2,4-D was unclassifiable.

Specific areas where the Panel either lacked consensus or had a difference in interpretation from that of the PMRA are listed below.

- The Panel did not agree with the PMRA's adopting the dog study as the basis for the overall preliminary risk assessment, citing various factors including issues related to allometric scaling, pharmacokinetics of 2,4-D in the rat and dog, uncertainty factor selection and the positions of both the USEPA and the European Commission on the dog and rat studies.
    - Subsequent to the PMRA's meeting with the 2,4-D Advisory Panel, the 2,4-D Task Force submitted additional data to the PMRA. These data provided the scientific evidence that was necessary to justify use of the rodent model rather than the dog model for human health risk assessment.
- The Panel did not agree with the PMRA's adopting the original chronic rat study for risk assessments, concluding that the more recent chronic rat study with a higher NOAEL would be more robust scientifically.
    - The PMRA maintains that the residual uncertainties concerning kidney toxicity in the 2,4-D database and the inability to resolve the differences in the two guideline studies warrant the use of the lower NOAEL set in the original rat study for risk assessment purposes. The PMRA has recently received additional data from the 2,4-D Task Force that may further influence the ADI. These data will be fully assessed during the re-evaluation of 2,4-D for agricultural use.
- The Panel did not accept the PMRA's default dermal absorption value used in the draft risk assessment, noting that the available studies consistently indicated a lower value than that adopted by the PMRA in its assessment.
    - The PMRA has lowered the dermal absorption factor for this assessment.
- The Panel indicated that childhood cancer issues should receive greater attention.
    - The PMRA maintains that a discussion of this issue is beyond the scope of this document, given the absence of data to show any specific association between 2,4-D exposure and childhood cancer as well as the lack of carcinogenic findings in the 2,4-D toxicological database.
    - Few studies address children's health effects from exposure to pesticides, and there are even fewer studies that address childhood cancer from exposure to specific pesticides. The majority of epidemiology studies focus on occupational groups, usually adult males, who are subject to multiple exposures. These exposures are not only to various pesticides but also to many other toxins and carcinogens at higher levels relative to the general population. Also, the exposure history for any population is often indirect, if available at all; the confounding

factors and covariates are often incompletely assessed. This further precludes any definitive cause-and-effect determinations. The examination of animal toxicity data from internationally accepted guideline studies using doses well above those to which humans are typically exposed, combined with exposure data obtained from well designed studies, is currently the best methodology available for assessing risks to human health.

Appendix II Risk assessment of human exposure: details of calculations

Table 1 Homeowner mixer/loader/applicator: short-term (1–7 day) exposure estimates and margins of exposure

Application equipment	Data source	Formulation /Rate	Area treated (ha/day)	Dermal unit exposure (µg/kg handled)[a]	Dermal exposure (µg/kg/day)[b]	Inhalation unit exposure (µg/kg handled)[a]	Inhalation exposure (µg/kg/day)[c]	Dermal MOE[d]	Inhalation MOE[d]	Combined MOE[e]
Residential lawns: homeowner wearing a short-sleeved shirt, short pants, no gloves Acid equivalent target: 1000										
Handheld equipment (low pressure)	ORETF	Liquid 1.75 kg a.e./ha	0.2	82741	41.37	23.7	0.12	725	253 000	723
			0.01		2.07		0.006	14500	5 060 000	14 500
Handheld equipment (low pressure)	ORETF	Liquid 1.25 kg a.e./ha	0.2	82741	29.55	23.7	0.085	1020	354 000	1010
			0.01		1.48		0.004	2030	7 090 000	2020
Ready-to-use hose-end sprayer	ORETF	Liquid 1.75 kg a.e./ha	0.2	6875	3.44	32.2	0.16	8730	186 000	8340
			0.01		0.17		0.008	175000	3 730 000	167 000
Dial-type hose-end sprayer	ORETF	Liquid 1.75kg a.e./ha	0.2	21 525	10.76	35.6	0.178	2790	169 000	2740
			0.01		0.54		0.009	55700	3 370 000	54 800
Backpack[f]	PHED	Liquid 1.75 kg a.e./ha	0.2	10 149	5.07	62.1	0.311	5910	96 600	5570
			0.01		0.25		0.016	118000	1 932 000	111 000
Push spreader	ORETF	Granular 1.75 kg a.e./ha	0.2	1378	0.69	1.72	0.009	43500	3 490 000	43 000
Residential lawns: homeowner wearing a short-sleeved shirt, long pants, no gloves Acid equivalent target: 1000										
Handheld equipment (low pressure)	ORETF	Liquid 1.75 kg a.e./ha	0.2	33 612	16.81	23.7	0.12	1790	253 000	1770
			0.01		0.84		0.006	35 700	5 060 000	35 500
Hose-end sprayer[g]	Harris 1991	Liquid 0.61 kg a.e./day	—	n/a	7.37 (dermal + inhalation)	n/a	n/a	n/a	n/a	4070
Rotary push spreader[h]	Harris 1991	Granular 1.2 kg a.e./day	—	n/a	0.62 (dermal + inhalation)	n/a	n/a	n/a	n/a	48400

[a] Median unit exposures are from ORETF, Best-fit unit exposures are from the PHED.

[b] Where dermal exposure µg/kg/day = (unit exposure × area treated × use rate × 10% dermal absorption)/bw. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 62 kg female body weight and female body surface areas.

[c] Where inhalation exposure µg/kg/day = (unit exposure × area treated × use rate)/ bw. Inhalation exposure based on a respiration rate of 17 litres per minute .

[d] Based on an oral NOAEL of 30 mg/kg/day, acid equivalent target is 1000.

[e] Calculated using the following equation: Combined MOE = NOAEL/(Exp_{DERMAL} + $Exp_{INHALATION}$)

Appendix II Risk assessment of human exposure: details of calculations

Table 1 Homeowner mixer/loader/applicator: short-term (1–7 day) exposure estimates and margins of exposure

Application equipment	Data source	Formulation / Rate	Area treated (ha/day)	Dermal unit exposure (µg/kg handled)[a]	Dermal exposure (µg/kg/day)[b]	Inhalation unit exposure (µg/kg handled)[a]	Inhalation exposure (µg/kg/day)[c]	Dermal MOE[d]	Inhalation MOE[d]	Combined MOE[e]
Residential Lawns: homeowner wearing a short-sleeved shirt, short pants, no gloves Acid equivalent target: 1000										
Handheld equipment (low pressure)	[illegible]	Liquid 1.5% Acid EQ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
			[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Handheld equipment (low pressure)	[illegible]	Liquid 1.5% Acid EQ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
			[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Pump-up sprayer (1 gallon)	[illegible]	Liquid 1.5% Acid EQ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
			[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Garden hose-end sprayer	[illegible]	Liquid 1.5% Acid EQ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
			[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Backpack	[illegible]	Liquid 1.5% Acid EQ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
			[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Push spreader	[illegible]	Granular 1.5% Acid EQ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Residential Lawns: homeowner wearing a short-sleeved shirt, long pants, no gloves Acid equivalent target: 1000										
Handheld equipment (low pressure)	[illegible]	Liquid 1.5% Acid EQ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
			[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Hose-end sprayer	[illegible]	Liquid 1.5% Acid EQ	[illegible]	n.a.	[illegible] dermal exposure	[illegible]	[illegible]	[illegible]	n.a.	[illegible]
Commercial applicator	[illegible]	Granular 1.5% Acid EQ	[illegible]	n.a.	[illegible] dermal exposure	[illegible]	[illegible]	[illegible]	n.a.	[illegible]

[a] Median unit exposure rates from ORETF, Reed-98 and exposure-one from the PHED.

[b] Where dermal exposure, µg/kg/day = unit exposure × area treated × absorption rate × 10³ ÷ dermal absorption (Dw. The 70 kg body weight and corresponding body surface area were used for both males and females as this [illegible] a similar exposure estimate to using a 60 kg female body weight and female body surface area.

[c] Where inhalation exposure, µg/kg/day = unit exposure × area treated × inhalation rate ÷ body weight. [illegible] used an exposure duration of 1 hr, respiration rate of 15 litres per minute.

[d] MOE = dermal NOAEL (1,000 mg/kg/day) ÷ dermal exposure (µg/kg/day) × 1000

[e] Combined MOE = 1/(1/dermal MOE + 1/inhalation MOE). Combined MOE = NOAEL (1) ÷ [illegible]

[f] The backpack application clothing scenario includes gloves. This data is not necessarily applicable to application on turf (USEPA 1997b, 2001)

[g] 90th percentile value from Harris (1991), based on homeowners applying 0.61 kg a.i./day with a hose-end sprayer, wearing long pants and short sleeves. Rate and area treated were not reported

[h] 90th percentile value from Harris (1991), based on homeowners applying 1.2 kg a.i./day of weed and feed with a rotary spreader. Rate and area treated were not reported.

Table 2 Adult and toddler acute (1 day) postapplication exposure and risk assessments on residential lawns

Scenario	Data source	Contact potential	Dermal exposure absorbed (µg/kg bw/day)[a]	Oral exposure (µg/kg/day)				Dermal MOE[e]	Oral MOE[e]	Combined MOE[f]
				Hand-to-mouth[b]	Turf mouthing[c]	Ingestion of soil[d]	Ingestion of granules			
Adult **Acid equivalent / BEE target: 300**										
Liquid 1.75 kg a.e./ha	USEPA 1997b, 2001	High	19.07	n/a	n/a	n/a	n/a	1311	n/a	1311
Liquid 1.1 kg a.e./ha	Harris 1991[g]	Low	8.24 (systemic)					3034		3034
Toddler **Acid equivalent / BEE target: 300**										
Liquid 1.75 kg a.e./ha	USEPA 1997b, 2001	High	31.91	23.3	0.73	0.08	n/a	2350	3107	1338
Granular[h] 1.75 kg a.e./ha	ORETF	High	31.91	23.3	0.73	0.08	148[b] max. value	2350	436	368
Granular[h] 1.75 kg a.e./ha	ORETF	High	31.91	23.3	0.73	0.08	81[b] min. value	2350	713	547

[a] Dermal exposure = %TTR × rate × TC × dermal absorption (10%) × duration / bw. Body weight (bw) is 70 kg for adults and 15 kg for toddlers. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 62 kg female body weight and female body surface areas. TTR is 2.63% based on the TTR study. TCs are 14 500 and 5 200 cm^2/hour for adults and toddlers respectively. Exposure duration is two hours. Rate expressed as acid equivalents = 17.5 µg/cm^2 for liquid and granular formulations.

[b] Based on 20 hand-to-mouth events/hour, 20 cm^2 surface area, saliva extraction factor (SEF) of 50%, dislodgeable foliar residue (DFR) is 5% of rate. Exposure = DFR × SA × hand-to-mouth events × SEF × 2 hours/15 kg bw

[c] Based on an ingestion of 25 cm^2 turf/day and an SEF of 50%, DFR is 5% of rate. Exposure = DFR × 25 × SEF/15 kg bw

[d] Based on an ingestion of 0.1 g soil/day, depth of 1 cm, 100% available/cm soil, 0.67 cm^3/g soil weight to volume conversion factor. Exposure = application rate × 0.1 × 0 67 × 1/15 kg bw

[e] Adult acute MOEs are based on a NOAEL of 25 mg/kg/day with a target of 300. Toddler acute MOEs are based on a NOAEL of 75 mg/kg/day with a target of 300.

[f] Combined MOE = NOAEL/(Exp_{DERMAL} + Exp_{ORAL})

[g] Based on adult bystanders wearing shorts, short-sleeved shirts and no shoes who were lying, sitting and walking on treated turf for one hour. Study was conducted at 1.1 kg/ha. Systemic exposure = 4.12 µg/kg/hr × 2 hr/day, where 4.12 µg/kg/hr is a 90th percentile based on a 1 hour restricted entry interval (REI).

[h] Maximum and minimum values based on an ingestion rate (IR) for dry pesticide formulations of 10% of the product applied in 1 ft^2. A low product application rate of 0.4166 kg fertilizer/100 m^2 corresponds to an ingestion rate of 3.7×10^4 µg with 6% 2,4-D per granule. A high product application rate of 15 kg fertilizer/100 m^2corresponds to an ingestion rate of 1.36×10^6 µg with 0.09% 2,4-D per granule. Exposure = IR × a.i./15 kg bw

[i] Calculations are based on TTR data for liquid formulation. Granular TTR would be much lower. The calculations is intended only to show that, even with such highly conservative assumptions, aggregate MOEs incorporating potential ingestion of granules are greater than the target MOE.

Table 3 Adult and toddler short-term (1–7 day) postapplication exposure and risk assessments on residential lawns

Scenario	Data source	Contact potential	Dermal exposure absorbed (µg/kg bw/day)[a]	Oral exposure (µg/kg/day)[e]			Dermal MOE[f]	Oral MOE[f]	Combined MOE[g]
				Hand-to-mouth[b]	Turf mouthing[c]	Ingestion of soil[d]			
Adult **Acid equivalent / BEE target: 1000**									
Liquid 1.75 kg a.e./ha	USEPA 1997b, 2001	High	2.54	n/a	n/a	n/a	11 811		11 811
Liquid 1.1 kg a.e./ha	Harris 1991[h]	Low	0.44 (systemic)				68 182		68 182
Liquid BEE 1.75 kg a.e./ha	USEPA 1997b, 2001	High	2.54				3937		3937
Liquid BEE 1.1 kg a.e./ha	Harris 1991[h]	Low	0.44 (systemic)				22 727		22 727
Toddler **Acid equivalent target: 300**									
Liquid 1.75 kg a.e./ha	USEPA 1997b, 2001	High	4.25	4.67	0.15	0.08	2944	2556	1368

[a] Dermal exposure = (%TTR × rate × TC × dermal absorption (10%) × duration) / bw. Body weight (bw) is 70 kg for adults and 15 kg for toddlers. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 62 kg female body weight and female body surface areas. TTR is 0.350% based on the TTR study. TCs are 14 500 and 5200 cm^2/hr for adults and toddlers, respectively. Exposure duration is two hours. Rates (acid equivalent) are 22.5 µg/cm^2 for liquids, 17.5 µg/cm^2 for 2,4-D BEE and 25 µg/cm^2 for granules.

[b] Based on 20 hand-to-mouth events/hour, 20 cm^2 surface area, SEF of 50%, DFR is 1% of rate. Exposure = DFR × SA × hand-to-mouth events × SEF × 2 hr/15 kg bw

[c] Based on an ingestion of 25 cm^2 turf/day and a saliva extraction factor (SEF) of 50%, DFR is 1% of rate. Exposure = DFR × 25 × SEF/15 kg bw

[d] Based on an ingestion of 0.1 g soil/day, depth of 1 cm, 100% available/cm soil, 0.67 cm^3/g soil weight to volume conversion factor. Exposure = application rate × 0.1 × 0.67 × 1/15 kg bw

[e] Ingestion of granules is not considered in the short-term scenario as this is an episodic rather than a typical exposure event.

Table 2 Adult and toddler acute (1 day) postapplication exposure and risk assessments on residential lawns

Scenario	Data source	Contact potential	Dermal exposure absorbed (µg/kg bw/day)[a]	Oral exposure (µg/kg/day)				Dermal MOE[c]	Oral MOE[c]	Combined MOE[c]
				Hand-to-mouth[b]	Turf mouthing[c]	Ingestion of soil[d]	Ingestion of granules			
Adult Acid equivalent; REI target: 300										
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]					[illegible]		[illegible]
Toddler Acid equivalent; REI target: 300										
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

Based on adult by standers wearing shorts, short-sleeved shirts and no shoes, after wearing clothing and coveralls contacted turf for one hour. Study was conducted at 11 kg/ha for 56 turfgrass experiments. 11 kg/ha is 1.1 kg/day, where 1.12 ng/kg hr is a 90th percentile hand-to-mouth transfer interval (HTI).

Maximum and minimum values based on an ingestion rate (IR) for dry pesticide formulations of 10% of the product applied in UR. A low product application rate of 0.1 oz/1,000 ft² (fertilizer 100) on turfgrass people weighing 70 kg ingestion rate of 1.7 × 10⁻⁵ mg with 6% 2,4-D per granule. A high product application rate of 1 lb/1,000 ft² (fertilizer 100) on turfgrass for an ingestion rate of 1.7 × 10⁻³ mg with 100% 2,4-D per granule. Ingestion IR = 1.6 × 10⁻⁴ kg/hr.

Calculations are based on UR data for liquid formulation. Granular UR would be much lower. The calculations are intended only to show that even with such highly conservative assumptions, aggregate MOEs incorporating potential ingestion of granules are greater than the target MOE.

Table 3 Adult and toddler short-term (1–7 day) postapplication exposure and risk assessments on residential lawns

Scenario	Data source	Contact potential	Dermal exposure absorbed (µg/kg bw/day)[a]	Oral exposure (µg/kg/day)[b]			Dermal MOE[c]	Oral MOE[c]	Combined MOE[c]
				Hand-to-mouth[d]	Turf mouthing[e]	Ingestion of soil[f]			
Adult Acid equivalent (AE) target 1000									
Liquid 1.1 kg AE/ha		Shirt							
Liquid 1.1 kg AE/ha		Vest							
Liquid 1.1 kg AE/ha		Shirt							
Liquid 1.1 kg AE/ha		Vest							
Toddler Acid equivalent target 300									
Liquid 1.1 kg AE/ha		Shirt							

Dermal exposure = AE × TR × ratio × IR × dermal absorption (10%) ÷ body weight (assumed 70 kg for adult and 15 kg for toddler). The 70 kg body weight and corresponding food consumption are used for both males and females as the result is a similar exposure estimate for males (1.7 L/kg body weight/day) and females (1.9 L/kg body weight/day). Used results for UR (mg/cm²) and TR (mg/cm²) and 24,000 cm² for adult and toddler surface area. Exposure duration = 1 day. Dermal absorption = 10% for liquid, 17% for granular.

Based on 20 hand-to-mouth events/hour, 20 min/waking day, SEI of 100%, HR for 1% of day.

Exposure = TOR × AV × frac. hand-to-mouth events × SEI × 20 min/h ÷ BW.

Based on an ingestion of 25 mg soil/day and a saliva extraction factor of 50% for 100% HR for 1% of day.

Exposure = TOR × 25 × SEI ÷ 15 kg bw.

Based on an ingestion of 0.1 mg soil/cm² (assumed 1 mg/cm² soil loading) for 100% HR for 1% of day.

Exposure = TOR × 0.1 × SEI ÷ 15 kg bw.

[f] Adult short-term MOEs are based on a NOAEL of 30 mg/kg/day and a target of 1000, with the exception of 2,4-D BEE where the MOE is based on the NOAEL of 10 mg/kg/day and a target of 1000. Toddler short-term MOEs are based on a NOAEL of 12.5 mg/kg/day with a target of 300.

[g] Combined MOE = NOAEL/(Exp_{DERMAL} + Exp_{ORAL})

[h] Based on adult bystanders wearing short, short-sleeved shirts and no shoes who were lying, sitting and walking on treated turf for one hour. Study was conducted at 1.1 kg/ha.
Systemic exposure = 0.22 µg/kg/hour × 2 hours/day, where 0.22 µg/kg/hour is a 90th percentile based on a 24-hour REI.

Table 4 Postapplication exposure and margins of exposure for golfers

Scenario	ACUTE EXPOSURE		SHORT-TERM EXPOSURE	
	Dermal exposure (µg/kg/day)[a]	Dermal MOE[b]	Dermal exposure (µg/kg/day)[a]	Dermal MOE[b]
Adults	**Acid equivalent target: 300**		**Acid equivalent / BEE target: 1000**	
Liquid: 1.75 kg a.e./ha	1.32	19011	0.18	171429
Liquid BEE: 1.75 kg BEE/ha	1.32	19011	0.18	57143
Youths	**Acid equivalent target: 300**		**Acid equivalent target: 300**	
Liquid all forms: 1.75 kg a.e./ha	2.36	31776	0.31	39796

[a] Dermal exposure = (%TTR × rate as acid equivalents (17.5 µg/cm^2) × TC × duration × dermal absorption) / bw. Body weight (bw) is 70 kg for adults and 39 kg for youths. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 62 kg female body weight and female body surface areas. The TC is 500 cm^2/hr based on generic transfer coefficients for turf. Duration is four hours. Acute TTR value (2.63 %) is based on the mean peak values and the short-term value (0.35 %) is based on a time weighted average over a seven-day period.

[b] Adult acute MOEs are based on a NOAEL of 25 mg/kg/day with a target of 300. Youth acute MOEs are based on a NOAEL of 75 mg/kg/day with a target of 300. Adult short-term MOEs are based on a NOAEL of 30 mg/kg/day and a target of 1000, with the exception of adult short-term MOEs for 2,4-D BEE, which are based on the NOAEL of 10 mg/kg/day and a target of 1000. Youth short-term MOEs are based on a NOAEL of 12.5 mg/kg/day with a target of 300.

Table 5 Short-term aggregate exposure and risk estimates for 2,4-D

Age group	Scenario	Dietary exposure (µg/kg/day)[a]	Exposure to homeowners applying 2,4-D to turf (µg/kg/day)		Exposure from re-entering treated turf (µg/kg/day)		Aggregate MOE[b]	DWLOC[c] (µg/L)
		Oral	Dermal[d]	Inhalation	Dermal	Oral		
Adult	Handheld (low-pressure) broadcast application	0.284	16.81	0.12	2.54	n/a	1519	359
	Ready-to-use hose-end broadcast application	0.284	3.44	0.16	5.53	n/a	4673	825
	Dial-type hose-end broadcast application	0.284	10.76	0.18	5.53	n/a	2180	568
	Backpack broadcast application	0.284	5.07	0.31	5.53	n/a	3656	763
	Push spreader application	0.284	0.69	0.009	5.53	n/a	8525	927
	Re-enter recreational areas treated with 2,4-D BEE	0.284	n/a	n/a	5.53	n/a	3544	251
	Golfing on turf treated with 2,4-D acid equivalent formulations	0.284	n/a	n/a	0.18	n/a	65 359	1034
	Golfing on turf treated with 2,4-D BEE formulations	0.284	n/a	n/a	0.18	n/a	21 786	334
Youth	Golfing on turf treated with 2,4-D	0.377	n/a	n/a	0.31	n/a	18 087	901
Toddler	Re-entering treated turf (Broadcast application)	0.71	n/a	n/a	4.25	4.89	1269	477

[a] Based on chronic dietary exposure estimates generated using DEEM®, does not include exposure to 2,4-D from drinking water.

[b] Adult aggregate MOEs are based on a NOAEL of 30 mg/kg/day and a target of 1000, with the exception of 2,4-D BEE MOEs, which are based on the NOAEL of 10 mg/kg/day and a target of 1000. Youth and toddler aggregate MOEs are based on a NOAEL of 12.5 mg/kg/day with a target of 300. Aggregate MOE = NOAEL/(Exp_{oral} + $Exp_{inhalation}$ + Exp_{dermal}) and does not include exposure to drinking water.

[c] The DWLOC is calculated as per the formula in section 4.0. Daily drinking water rate is 2 L/day for adults and youth, and 1 L/day for toddlers

[d] Based on short-sleeved shirts, shorts and no gloves, except for handheld (low-pressure) broadcast applications where based on long pants, short-sleeved shirt, no gloves.

Adult short-term MOE are based on a NOAEL of 10 mg/kg/day and a target of 1000, with the exception of 2,4-D BEE where the MOE is based on the NOAEL of 10 mg/kg/day and a target of 1000. Toddler short-term MOE are based on a NOAEL of 12 mg/kg/day with a target of 300.

Combined MOE = NOAEL/(Application + Exposure)

Based on adult hypothetical maximum application rate of 1.4 lb ai/A and no more than eight hours of mixing and loading on treated turf on day one. Short-term exposure: 2,4-D LE/ha

Short-term exposure = 0.75 µg/kg/lb ai × 2.8 lb ai/A × 1000 µg/mg × 0.27 mg/kg/hour × 8 hr/day = 4,536 µg/kg/day (rounded) for 2,4-D LE/ha

2,4-D BEE

Table 4 Postapplication exposure and margins of exposure for golfers

Scenario	ACUTE EXPOSURE		SHORT-TERM EXPOSURE	
	Dermal exposure (µg/kg/day)[a]	Dermal MOE[b]	Dermal exposure (µg/kg/day)[a]	Dermal MOE[b]
Adults	Acid equivalent target: 300		Acid equivalent – BEE target: 1000	
Liquid, 1.33 oz ai/A	0.43	1000	0.43	10,000
Liquid/DF, 1.33 oz ai/A	0.43	1000	0.43	10,000
Youths	Acid equivalent target: 300		Acid equivalent target: 300	
Liquid/Granular, 1 oz ai/A	0.43	1000	0.43	10,000

[a] Dermal exposure = (% LHR × rate as acid equivalent) (17.5 µg/cm²). To calculate dermal exposure by: Body weight (bw) is 70 kg for adults and 39 kg for youths. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 60 kg female body weight and female body surface areas. The DFR 500 cm² is based on generic transfer coefficients for turf. Duration is four hours. Acute LHR value (2.6) % is based on the mean peak values and the dermal rate value of 1.4 % is based on a time-weighted average over a seven-day period. Adult acute MOE are based on a NOAEL of 25 mg/kg/day with a target of 300. Youth acute MOE are based on a NOAEL of 75 mg/kg/day with a target of 300. Adult short-term MOE are based on a NOAEL of 10 mg/kg/day and a target of 1000, with the exception of adult short-term MOE for 2,4-D BEE, which are based on the NOAEL of 10 mg/kg/day and a target of 1000. Youth short-term MOE are based on a NOAEL of 12.5 mg/kg/day with a target of 300.

Table 5 Short-term aggregate exposure and risk estimates for 2,4-D

Age group	Scenario	Dietary exposure (ng/kg/day)[1]	Exposure to homeowners applying 2,4-D to turf (ng/kg/day)		Exposure from re-entering treated turf (ng/kg/day)		Aggregate MOE	DWLOC[2] (ng/L)
		Oral	Dermal[3]	Inhalation	Dermal	Oral		
Adult	Broadcast liquid application (2,4-D LO/EHE)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Push/stop broadcast liquid application	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Backpack broadcast liquid application	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Backpack broadcast application	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Push spreader application	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Residue (golf course) on treated with 2,4-D EHE	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Golfing on turf treated with 2,4-D acid/amine dimethylamine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Golfing on turf treated with 2,4-D EHE formulation	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Youth	Golfing on turf treated with 2,4-D	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Toddler	Scenarios listed for broadcast application	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[1] Based on chronic dietary exposure estimate generated using DEEM™ does not include exposure to 2,4-D from drinking water.

Adult aggregate MOEs are based on a NOAEL of 50 mg/kg/day and a target of 1000, with the exception of 2,4-D EHE MOEs, which are based on the NOAEL of 10 mg/kg/day and a target of 1000. Youth and toddler aggregate MOEs are based on a NOAEL of 12.5 mg/kg/day with a target of 100. Aggregate MOE = NOAEL/(Exp$_{oral}$ + Exp$_{dermal}$ + Exp$_{inhalation}$) and does not include exposure to drinking water.

[2] The DWLOC was calculated as per the formula in Section 4.0, Daily drinking water use is 2 L/day for adults and youth and 1 L/day for toddlers.

[3] Based on short-sleeved shirt, short- and no gloves (except for handheld liquid/open-cab) Broadcast application (Shirt based on long pants, short-sleeved shirt, no gloves).

Table 6 Commercial mixer/loader/applicator: short-term exposure estimates and margins of exposure for turf

Application equipment	Data source[a]	Formulation/ Rate	Area treated (ha/day)	Dermal unit exposure (µg/kg handled)	Dermal exposure (µg/kg/day)[b]	Inhalation unit exposure (µg/kg handled)	Inhalation exposure (µg/kg/day)[c]	Dermal MOE[d]	Inhalation MOE[d]	Combined MOE[e]
Residential lawns: commercial lawn care operator wearing long pants, long-sleeved shirt, gloves (1–30 days) Acid equivalent / BEE target MOE = 1000										
Low-pressure turf gun	ORETF	Liquid 1.75 kg a.e./ha	2	785	3.93	4	0.2	7643	150 000	7273
Backpack[f]	PHED		0.4 (spot)	5446	5.45	62.1	0.62	5509	48 309	4945
Low-pressure turf gun	ORETF	Liquid BEE 1.75 kg a.e./ha	2	785	3.93	4	0.2	2548	50 000	2424
Backpack[f]	PHED		0.4 (spot)	5446	5.45	62.1	0.62	1836	16 103	1648
Low-pressure turf gun	ORETF	Wettable powder (water soluble packaging) 1.17 kg a.e./ha	2	1427	4.77	14.5	0.48	6289	61 892	5709
Low-pressure turf gun	ORETF	Wettable powder (water soluble packaging) 1.058 kg a.e./ha	2	1290	3.9	47.8	1.44	7693	20 762	5613
"Typical"	Harris 1991[g]	Liquid 1.4 kg a.e./day	not reported	n/a	4.9 (systemic)	n/a	n/a	n/a	n/a	6122
Golf courses and sod farms: commercial mixer/loader/applicator wearing long pants, long-sleeved shirt and gloves (1–7 days) Acid equivalent / BEE target MOE = 1000										
Low-pressure turf gun	ORETF	Liquid 1.75 kg a.e./ha	2	785	3.93	4	0.2	7643	150 000	7273
Backpack[f]	PHED		0.4 (spot)	5446	5.45	62.1	0.62	5509	48 309	4945
Groundboom (golf)	PHED		16	83.6	3.34	2.6	1.04	8971	28 846	6843
Groundboom (sod)			30	83.6	6.27	2.6	1.95	4785	15 385	3650

Application equipment	Data source[a]	Formulation/ Rate	Area treated (ha/day)	Dermal unit exposure (µg/kg handled)	Dermal exposure (µg/kg/day)[b]	Inhalation unit exposure (µg/kg handled)	Inhalation exposure (µg/kg/day)[c]	Dermal MOE[d]	Inhalation MOE[d]	Combined MOE[e]
Low-pressure turf gun	ORETF	Liquid BEE 1.75 kg a.e./ha	2	785	3.93	4	0.2	2548	50 000	2424
Backpack[f]	PHED		0.4 (spot)	5446	5.45	62.1	0.62	1836	16 103	1648
Groundboom (golf)	PHED		16	83.6	3.34	2.6	1.04	2990	9615	2281
Groundboom (sod)			30	83.6	6.27	2.6	2.6	1595	5128	1217
Low-pressure turf gun	ORETF	Wettable powder (water soluble packaging) 1.17 kg a.e./ha	2	1427	4.97	14.5	0.48	6289	61 892	5709
Groundboom (golf)	PHED		16	54.1	1.45	1.14	0.3	20 736	98403	17 127
Groundboom (sod)			30	54.1	2.71	1.14	0.57	11 059	52 482	9134
Low-pressure turf gun	ORETF	Water dispersible granule 1.058 kg a.e./ha	2	1290	3.9	47.8	1.44	7693	20 762	5613
Groundboom (golf)	PHED		16	196	4.74	2	0.48	6329	62 027	5743
Groundboom (sod)			30	196	8.89	2	0.91	3376	33 081	3063

[a] Median unit exposures are from ORETF, Best-fit unit exposures are used from the PHED.

[b] Where dermal exposure µg/kg/day = (unit exposure × area treated × use rate [expressed as acid equivalents]) × 10% dermal absorption)/ bw. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 62 kg female body weight and female body surface areas.

[c] Where inhalation exposure µg/kg/day = (unit exposure × area treated × use rate [expressed as acid equivalents]) / bw. Inhalation exposure based on a respiration rate of 17 litres per minute.

[d] 1–30 day short-term MOEs are based on a NOAEL of 30 mg/kg/day and a target of 1000, with the exception of short-term MOEs for 2,4-D BEE, which are based on a NOAEL of 10 mg/kg/day and a target of 1000.

[e] Combined MOE = NOAEL/(Exp_{DERMAL} + $Exp_{INHALATION}$)

[f] Backpack data may not be completely applicable for application to lawns (USEPA 1997b).

[g] Biomonitoring data (Harris 1991). 90th percentile used due to study limitations. Represents "typical" professional applicator exposure. Applied approximately 1.4 kg a.e./day; personal protective equipment not specified.

Table 6 Commercial mixer/loader/applicator: short-term exposure estimates and margins of exposure for turf

Application equipment	Data source[a]	Formulation/ Rate	Area treated (ha/day)	Dermal unit exposure (ug/kg handled)	Dermal exposure (ug/kg/day)[b]	Inhalation unit exposure (ug/kg handled)	Inhalation exposure (ug/kg/day)[c]	Dermal MOE[d]	Inhalation MOE[e]	Combined MOE[f]
Residential lawns: commercial lawn care operator wearing long pants, long-sleeved shirt, gloves (1–30 days) Acid equivalent – BEE target MOE = 1000										
Low-pressure turf gun	WBEH	Liquid 1.79 kg a.e./ha	8	363	4.94	4	0.2	7643	150 000	3771
Backpack	PBEH		0.4 (goal)	446	6	67.1	0.62	5097	48 309	1443
Low-pressure turf gun	WEEH	Liquid DEL 1.79 kg a.e./ha	8	280	3.81	4	0.2	2548	301 607	2424
Backpack	PBED		0.4 (goal)	5446	5.43	67.1	0.62	1836	16 191	1648
Low-pressure turf gun	WBEH	Wettable powder water-soluble packaging 1.17 kg a.e./ha	8	1427	1.77	134	0.48	6288	61 497	3701
Low-pressure turf gun	OBEH	Wettable powder water-soluble packaging 1.079 kg a.e./ha	8	1290	1.6	47.8	1.44	7631	20 762	3611
Topical	Harris (1991)	Liquid 1.8 kg a.e./day	n/a reported	n/a	1.9 (x/dermis)	n/a	n/a	825	165	8125
Golf courses and sod farms: commercial mixer/loader/applicator wearing long pants, long-sleeved shirt and gloves (1–7 days) Acid equivalent – BEE target MOE = 1000										
Low-pressure turf gun	WBEH	Liquid 1.79 kg a.e./ha	8	363	4.94	4	0.2	7643	150 000	3771
Backpack	PBED		0.4 (goal)	5446	5.43	67.1	0.62	1836	16 191	1648
Tractor-mounted (cab)	TBEH		16	874	1.41	5.6	1.94	8951	25 816	4813
Tractor-mounted (cab)			40	3494	6.77	5.6	1.94	1790	5163	1000

Application equipment	Data source[a]	Formulation/ Rate	Area treated (ha/day)	Dermal unit exposure (µg/kg handled)	Dermal exposure (µg/kg/day)[b]	Inhalation unit exposure (µg/kg handled)	Inhalation exposure (µg/kg/day)[c]	Dermal MOE[d,f]	Inhalation MOE[e,f]	Combined MOE[g]
Tractor, open cab, mixer/loader	WBEC (B)	Liquid DCE (1 kg a.s./ha)	97	763	1.011	4	0.37	2540	810000	1124
Backpack	PHED		0.4 (0.03)	5446	7.215	6.03	0.498	1800	20482	1660
Groundboom, closed (wide)	PHED		36	4376	5.797	7.6	1.01	2586	9653	2181
Groundboom, closed			80	13346	17.679	2.62	2.62	1087	3128	1127
Tractor, open cab, fan cab	CWCTF	Wettable powder (water soluble packaging) 1.17% AI/ha (kg)	97	1127	4.87	11.5	0.18	6289	61897	5700
Groundboom, closed	PHED		36	34.1	1.35	1.14	0.5	20300	19300	11137
Groundboom, open			80	34.1	3.0	1.43	0.57	11000	17482	9141
Tractor, open cab, fan cab	PHED	Water dispersible granule 1.054 kg ai/ha	97	1350	5.8	17.6	1.31	5603	25126	4411
Groundboom, closed			37	1.16	1.34	3	0.18	6450	6.398	5.31
Groundboom, open			80	190	8.83	3.5	0.84	3450	14.084	3001

[a] Median unit exposures are from ORETF. Best fit unit exposures are used from the PHED.

[b] Where dermal exposure (µg/kg/day) = (unit exposure) × (area treated) × (use rate [expressed in acid equivalents]) × 10% dermal absorption factor. The 70 kg body weight and corresponding body surface area were used for both males and females as this results in a similar exposure estimate to using a 60 kg female body weight and female body surface area.

[c] Where inhalation exposure (µg/kg/day) = (unit exposure) × (area treated) × (use rate [expressed in acid equivalents]) × (a.s. Inhalation exposure based on an exposition rate of 15 litres per minute.

[d] 30 day short-term MOEs are based on a NOAEL of 10 mg/kg/day and a target of 1000, with the exception of short-term MOEs for 2,4-D BEE, which are based on a NOAEL of 10 mg/kg/day and a target of 1000.

[e] Combined MOE = NOAEL (a.s.)/(exposure (a.s.) + exposure (a.s.))

[f] Backpack data may not be completely applicable for application to lawns (USEPA 1997b).

[g] Biomonitoring data (Harris, 1991) 90th percentile used due to study limitations. Represents "typical" professional applicator exposure. Applied approximately 1.4 kg a.s./day, personal protective equipment not specified.

Table 7 Worker postapplication exposure and risk on golf course and sod farm turf

Scenario	ACUTE EXPOSURE [a]			SHORT-TERM EXPOSURE [a]		
	% TTR [b]	Dermal Exposure [c] µg/kg/day	MOE	% TTR [b]	Dermal Exposure [c] µg/kg/day	MOE
Scouting, broadcast, pruning, scouting, mowing Target: 300 Target: 1000						
Liquid 1.75 kg a.i./ha	2.6%	303	8300	0.43%	50	50 000
Liquid HEC 1.75 kg a.i./100 L/ha	2.6%	303	8300	0.43%	50	50 000
Harvesting and transplanting treated turf Target: 300 Target: 1000						
Liquid 1.75 kg a.i./ha	24.0%	2800	900	0.43%	50	5000
Liquid HEC 1.75 kg a.i./100 L/ha	24.0%	2800	900	0.43%	50	5000
Liquid 0.84 kg a.i./ha	24.0%	2800	900	0.43%	50	5000
Liquid HEC 1.75 kg a.i./100 L/ha	24.0%	2800	900	0.43%	50	5000
Liquid 1.75 kg a.i./ha	24.0%	2442	1000	0.43%	50	6000
Liquid HEC 1.75 kg a.i./100 L/ha	24.0%	2442	1000	0.43%	50	6000

[a] Acute MOEs are based on a NOAEL of 25 mg/kg/day with a target of 300. Short-term MOEs are based on a NOAEL of 40 mg/kg/day and a target of 1000, with the exception of 2,4-D HEC, where MOEs are based on the NOAEL of 10 mg/kg/day and a target of 1000.

[b] Chemical-specific data from a turf transferable residue and dissipation study. Acute TTR value is based on the mean peak values and the short-term value is based on a time-weighted average over a seven-day period. The day 7 TTR value is 0.148% of the applied rate.

[c] Dermal exposure = % TTR × rate in acid equivalents 17 × µg/cm² for liquids and 17.5 µg/cm² for liquid 2,4-D HEC) × 1% × 8 hours × 10% dermal absorption ÷ bw. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 65 kg female body weight and female body surface area. 1% and 10% are SOPs for the turf transferable activities. New exposure data may be used to refine the exposure estimates.

Table 7 Worker postapplication exposure and risk on golf course and sod farm turf

Scenario	ACUTE EXPOSURE[a]			SHORT-TERM EXPOSURE[a]		
	% TTR[b]	Dermal Exposure[c] µg/kg/day	MOE	% TTR[b]	Dermal Exposure[c] µg/kg/day	MOE
Aerating, fertilizing, pruning, scouting, mowing	**Target: 300 Target: 1000**					
Liquid 1.75 kg a.e./ha	2.63%	2.63	9506	0.35%	0.35	85 714
Liquid BEE 1.75 kg BEE/ha	2.63%	2.63	9506	0.35%	0.35	28 571
Harvesting and transplanting treated turf	**Target: 300 Target: 1000**					
Liquid 1.75 kg a.e./ha	2.63%	88.79	288	0.35%	11.55	2579
Liquid BEE 1.75 kg BEE/ha	2.63%	88.79	288	0.35%	11.55	866
Liquid 1.55 kg a.e./ha	2.63%	79.88	313	0.35%	10.23	2933
Liquid BEE 1.55 kg BEE/ha	2.63%	79.88	313	0.35%	10.23	978
Liquid 1.25 kg a.e./ha	2.63%	64.42	388	0.35%	8.25	3636
Liquid BEE 1.25 kg BEE/ha	2.63%	64.42	388	0.35%	8.25	1212

[a] Acute MOEs are based on a NOAEL of 25 mg/kg/day with a target of 300. Short-term MOEs are based on a NOAEL of 30 mg/kg/day and a target of 1000, with the exception of 2,4-D BEE, where MOEs are based on the NOAEL of 10 mg/kg/day and a target of 1000.

[b] Chemical-specific data from a turf transferable residue and dissipation study. Acute TTR value is based on the mean peak values and the short-term value is based on a time-weighted average over a seven-day period. The day 3 TTR value is 0.148% of the applied rate.

[c] Dermal exposure = % TTR × rate as acid equivalents 17.5 µg/cm^2 for liquids and 17.5 µg/cm^2 for liquid 2,4-D BEE) × TC × 8 hours × 10% dermal absorption / bw. The 70 kg body weight and corresponding body surface areas were used for both males and females as this results in a similar exposure estimate to using a 62 kg female body weight and female body surface areas. TCs are 500 and 16 500 cm^2/hour for the various re-entry activities. New exposure data may be used to refine these estimates of exposure.

References

A list of additional information regarding 2,4-D is included below. This is limited to a subset of published studies including review articles and international regulatory documents. It is not an exhaustive listing of all published studies on 2,4-D. Other relevant information referenced within each of the published reviews and international documents were also considered in this re-evaluation and these documents may be consulted for further reference listings. This list does not include references to the unpublished proprietary data utilized in this assessment.

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